HUMAN REPRODUCTION

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* Reproduction

· Reproduction is a process by which an organism give rise to offspring.

Reproduction

Sexual	A-sexual
→ 2 parents are involved	→ only one parent
→ fusion of gametes	→ No fusion & form of gamete
→ formation of zygote	→ No formation of zygote
eg: Human	eg: Binary fission

Q. Why reproduction is important?
→ To continue population of species on earth, reproduction is important.

* Types of sexual organism
(on the basis of development & production of foetus)

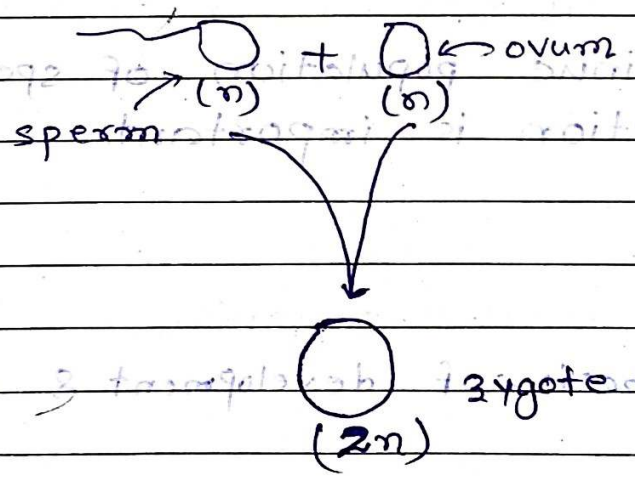
(1) Viviparous
→ Organism that give birth to young ones

(2) Oviparous
→ Organism that lay egg(s)

(3) Ovoviviparous
→ Organism in which the egg(s) develops hatch inside the mother body, but young ones born.

∴ Human are sexually reproducing and viviparous organism

* Gamete
→ sex cell, haploid (n) in nature
→ ♂ gamete → sperm
→ ♀ gamete → ovum (pl. ova)



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* Reproductive events in human

- There are six reproductive events in human

(1) Gametogenis
→ formation of gamete
- formation of sperm (male gamete) → spermatogensis
- formation of ova (♀ gamete) → Oogenesis

(2) Insemination
→ Tranfer of sperm in female genital tract is known as insemination

(3) fertilization / syngamy
→ fusion of male and female gamete to form zygote is called fertilization.

→ In human fertilization is internal (inside female body)

(4) Implantation

zygote → 2-celled stage → 4-celled stage → 8-16 celled stage (MORULA)

→ Blastocyst

- Inplantation stage include formation and development of blastocyst and attachement to the uterus wall (endometrium)

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- When blastocyst fully embbed (attached) to the uterus wall, it is known as embryo.

(5) Gestation
→ period of embryonic development
→ Organogenesis (formⁿ of organ) take place
→ In human, it is of 9 months

(6) Parturition
→ Delivery of fully developed foetus.

Note:- (i) To maintain ploidy of zygote after fertilization, gametes are haploid in nature

(ii) Sperm formation starts at puberty and continue to the dead.

(iii) Ovum formation starts at embryonic development and stop around the age of fifty years

* Sex organ

Sex organ
- primary sex organ
- Seconday sex organ

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- Primary sex organ
→ essential sex organ
→ Gametogenesis take place
→ Release sex hormone
→ ♂ → testes } Developed from mesoderm
→ ♀ → ovary

- Secondary sex organ
→ Also called accessory sex organ
→ accessory duct, accessory gland and external genitals
→ Help in tranfer of gamete

* Secondary sex organ in ♂

(1) Accessory ducts
- It include :- rete testis, vasa efferentia, vas deferens, epididymis and urethra.

(2) Accessory glands
- It includes :- seminal vesicle, prostate and bulbourethral/cower's gland

(3) External genitals
- It include :- scrotum and ~~testie~~ penis

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* Secondary sex organ in female

(1) Accessory ducts
- It include :- fallopian tube/oviduct, uterus, cervix and vagina

(2) Accessory glands
- It include :- Bartholin's gland and mammary gland.

(3) External genital
- It include :- vulva

* Male reproductive system

- Located in pelvis region
- It is consist of :- pair of testes, accessory ducts, accessory gland and external genitalia

* Testes

- primary sex organ, one-pair, oval shape
- In adult, length = 4-5cm, width = 2-3cm
- Located outside abdominal cavity, in a pouch called scrotum
- Scrotum provide 2-2.5°C less tem. than body tem to testes for spermatogenesis.

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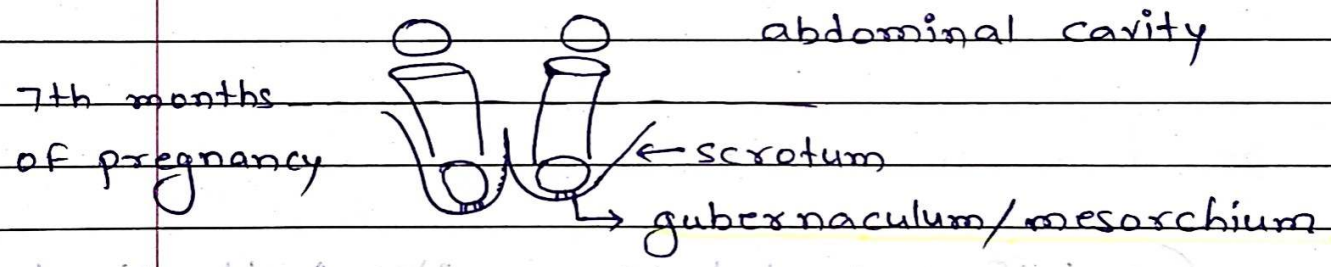
Extra

- During embryonic life, tetes is present in abdominal cavity. In 7th months of pregnancy, testes decend down in scrotum (outside the abdominal cavity) through inguinal canal.

- If testes failed to descend in scrotum, this condition is known as cryptochildism (lead to sterility). To treat cryptochildism, Orchiopexy is done
  ↳ through surgery testes is descend in scrotum



- Testes is attached to scrotum through gubernaculum

- For thermoregulation, scrotum has Dartos muscle and Cremaster muscle. During summer, these muscles, ~~contract~~ relax and move testes away from body. During winter, these muscles contract and move testes towards body.

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* Internal structure of testes

- There are three covering of testes
  (i) Tunica vaginalis [outermost, double, incomplete]
  (ii) Tunica Albuginea [middle, thick]
  (iii) Tunica vascularis [innermost, provide blood supply]
- Each testis has 250 compartments called testicular lobules. Septum of testicular lobules is formed by Tunica Albuginea
- In each testicular lobule 1-3 seminiferous tubules are present where spermatogenesis occur

* T.S of testies

- Seminiferous tubule on its inside lined by two types of cells.

(i) Spermatogonia or male germ cell or sperm mother cell (cuboidal cell)
→ Undergo meiotic (meiosis) division to form sperm

(ii) Sertoli cell or Nurse cell or subtentacular cell (columnar cell)
→ provide nourishment to germ cell
→ form blood testes barrier

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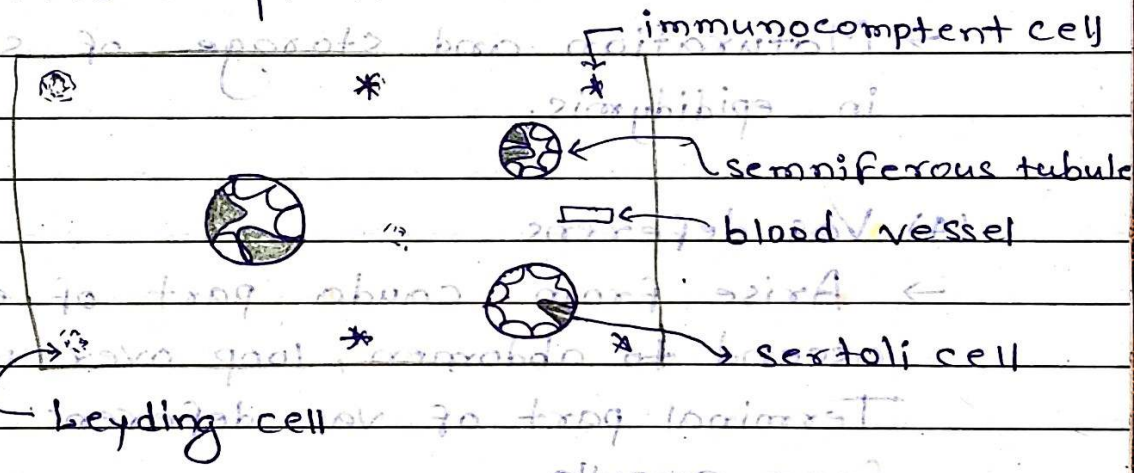
→ provide anti-mullerian factor
→ provide Androgen binding protein

- The space outside seminiferous tubule is called Interstital space

- Interstital space contain:-
(a) Leydig cell / Interstital cell
↳ provide androgen, mainly testosterone
(b) Small blood vessels
(c) Immuno comptent cell



T.S of testes (testicular lobule)

* Male accessory duct

(1) Rete testies
→ Network formed by end part of semiferous tubule (straight structure) is called rete testis

(2) Vasa efferentia / Efferent ductule

→ Carry sperm from rete testes to epididymis

→ It leave testis

(3) Epidymis

→ 6m long, coiled tube located on posterior side of each testis.

→ It has three parts :- (i) Caputa epididymis (head) (ii) Corpus epididymis (body) and (iii) Cauda epididymis (tail)

→ Maturation and storage of sperm occurs in epididymis.

(4) Vas deferens

→ Arise from cauda part of epididymis and ascend to abdomen, loop over urinary bladder. Terminal part of vas deferens is dilate and form ampulla.

→ Ampulla recieve duct from seminal vesicle and form ejaculatory duct.

· Ejaculatory duct open into urethra

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Urethra (3 parts)

(i) prostatic urethra (ii) membranous urethra (iii) penile urethra

- Sperm travel through urethra/ uringgential duct and comes out through an opening called urethral meatus.

* Male accessory glands

There are three male accessory glands in male which release seminal plasma

(1) Seminal vessicle

→ paired structure
→ present at junction of vas deferens and prostate, Behind urinary bladder
→ Secrete seminal fluid which is slightly alkaline in nature. (pH ≈ 7.3)
→ Seminal fluid contain fructose, certain enzymes (fibringen, prostaglandin)
→ Contribute 60-70% of semen

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(2) Prostate gland
→ Unpaired structure
→ located below urinary bladder/ at the origin of urethra.
→ Secrete prostatic fluid which is slightly acidic in nature (pH = 6.5)
→ prostatic fluid contain citric acid, Ca^{2+}, It help in maturation & mobility of sperm.

(3) Bulbourethral gland
→ Also known as Cower's gland
→ paired structure
→ Beneath prostate, behind urethra
→ During sexual activity, it helps in lubrication of penis.
→ Slightly alkaline (pH = 7.2)

* Semen
→ Semen = sperm + seminal plasma (fluid part of semen secreted by accessory glands) rich in fructose, calcium & certain enzymes.
→ Slightly alkaline pH
→ During single ejaculation, male release 200 – 300 million sperm.
→ 3-4 ml semen is released
→ For normal male fertility 60% of ejaculated sperm should have normal shape and size. And 40% of them must have vigrous motility
→ Sperm count = 22 – 120 million/ml

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* Male external genitalia

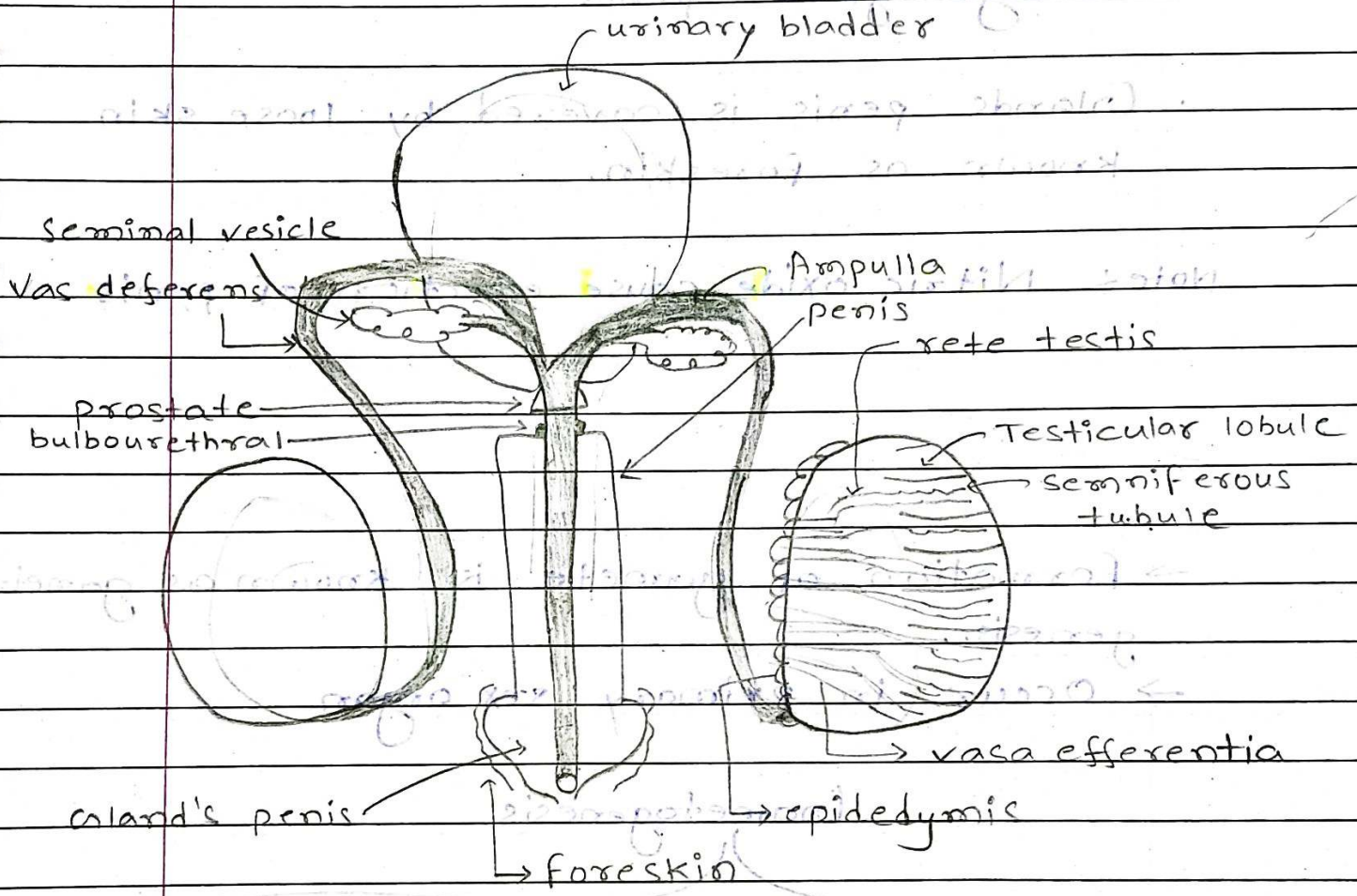

Diagram of male reproductive system

- Penis is the male external genitalia through which copulation is done.
- Penis has special erectile tissue which help in insemination.
- The large end part of penis is known as glands penis.

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- During erection, blood flow in vessels increase which cause erect penis and enlarge glands penis.

- Glands penis is covered by loose skin known as foreskin.

Note :- Nitric oxide cause erection of penis.

* Gametogenesis

→ formation of gamete is known as gametogenesis.
→ Occur in primary sex organ.

Gametogenesis

(i) Spermatogenesis (ii) Oogenesis

(1) Spermatogensis
→ Occur in male
→ location :- in testes (seminiferous tubule)
→ formation of sperm is known as spermatogensis.
→ Contine even in old age

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(2.) Oogenesis
→ Occur in female
→ location - ovary
→ formation of ova is known as oogenesis
→ start during intra uterine life/embryonic stag
→ end at menopause (around 45-50 year age)

* Stage of gametogenesis

• Three 3 Stage in gametogenesis.

(i) Multiplication phase
→ In this phase, spermatogonia or oogonia divide mitotically and increase their number

(ii) Growth phase
→ ~~primam~~ primary spermatocyte and primary oocyte is form by cytoplasmic growth.

(iii) Maturation phase
→ In this phase, maturation take place

* Spermatogenesis

→ Spermatogonia/sperm mother cell/male germ cell divide mitotically and increase their number [Multiplication phase]

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→ few spermatogonia grow in size and form primary spermatocyte (growth phase)

→ primary spermatocyte undergo meiotic I (reductional division) to form 2 equal, haploid, secondary spermatocytes (chromosome number gets halved)

→ Secondary spermatocytes undergo meiotic II (equational division) to form 2 equal, haploid spermatids (chromosome number remain same)

→ Spermatid tranform into spermatozoa by the process spermiogenesis.

→ The head of spermatozoa got embbed in Sertoli cell and derive nutrition from it. After that it get release from seminiferous tubule. This is known as spermiation

→ Longest phase in spermatogenesis - Maturation phase

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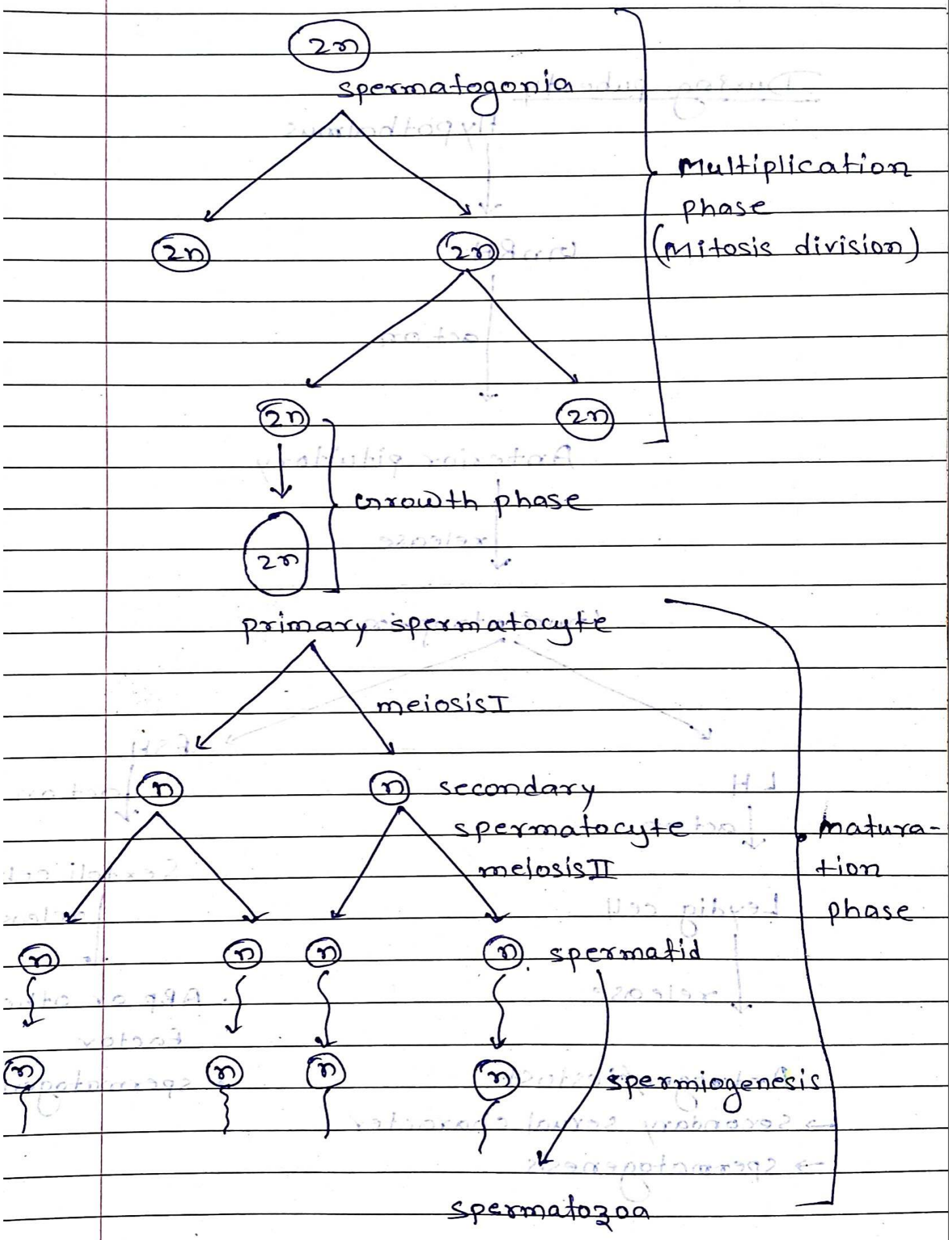
2n
spermatogonia
2n
2n
2n
2n
Multiplication phase (Mitosis division)
2n
growth phase
2n
primary spermatocyte
meiosis I
n
n
secondary spermatocyte
meiosis II
n
n
n
n
spermatid
n
n
n
n
spermiogenesis
spermatozoa
Matura-tion phase

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* Hormonal regulation in spermatogenesis

During puberty

Hypothalmus
↓
GnRH
↓ act on
Anterior pituitory
↓ release
Gonadotrophin

→ LH
↓ act on
Leydig cell
↓ release
Antrogen/testostrone
→ Secondary sexual character
→ spermatogenesis

→ FSH
↓ act on
Sertoli cell
↓ release
ABP or other factor
spermatogenesis

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- Excess spermatogenesis cause release of Inhibin from sertoli cell which give -ve feedback to hypothalmus & Anterior pituitary

- Excess spermatogenesis will give -ve feedback to hypothalmus & anterior pituitary from Leydig cell

* Structure of sperm

→ Microscopic structure
→ consist of 4 parts :- Head, neck, middle piece and tail.

(1) Head
→ Anterior part of head has cap like structure called acrosome
→ Acrosome is filled with enzyme (sperm lysin) that help in penetrating the protective covering of ova.
→ Acrosome is formed by condensation of golgi body
→ posterior part of head has haploid elongated nucleus

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(2) **Neck**

→ Short part b/w head and middle piece

→ It has 2 centriole

proximal centriole
→ Help in divⁿ of zygote

Distal centriole
↳ form axial filament

(3) **Middle piece**

→ Known as energy chamber of sperm b/c it has numerous (25-30) mitochondria which provide energy for motility of sperm

→ The mitochondria is arranged spirally which forms **Nebenkern sheath**.

(4) **Tail**

→ provide motility to sperm

note:- 46/23 pair

22 pair outsome
→ same in ♂ & ♀

one pair allosome/sex chromosome different in male and female
♂ = XY
♀ = XX

ova (X)

sperm (X) (Y)

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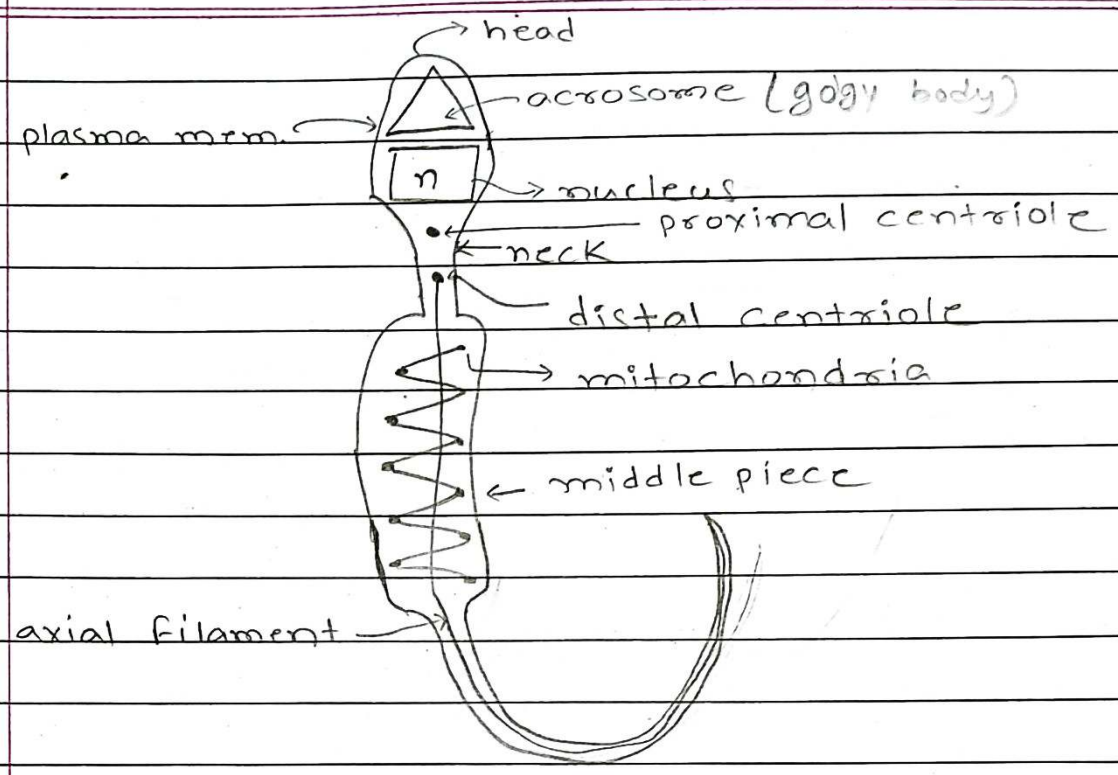

Structure of sperm

* Female reproductive system

- It consist of primary sex organ (ovary), ♀ accessory duct (fallopian tube, uterus, cervix, vagina). ♀ accessory gland and ♀ ~~etc~~ external genitalia known as vulva (mons pubis, Labia majora, Labia minora, clitoris, hymen)

Note :- Along with these, one pair of mammary glands, structurally & functionally support ovulation, fertilisation, pregnancy ~~&~~, childbirth & child care

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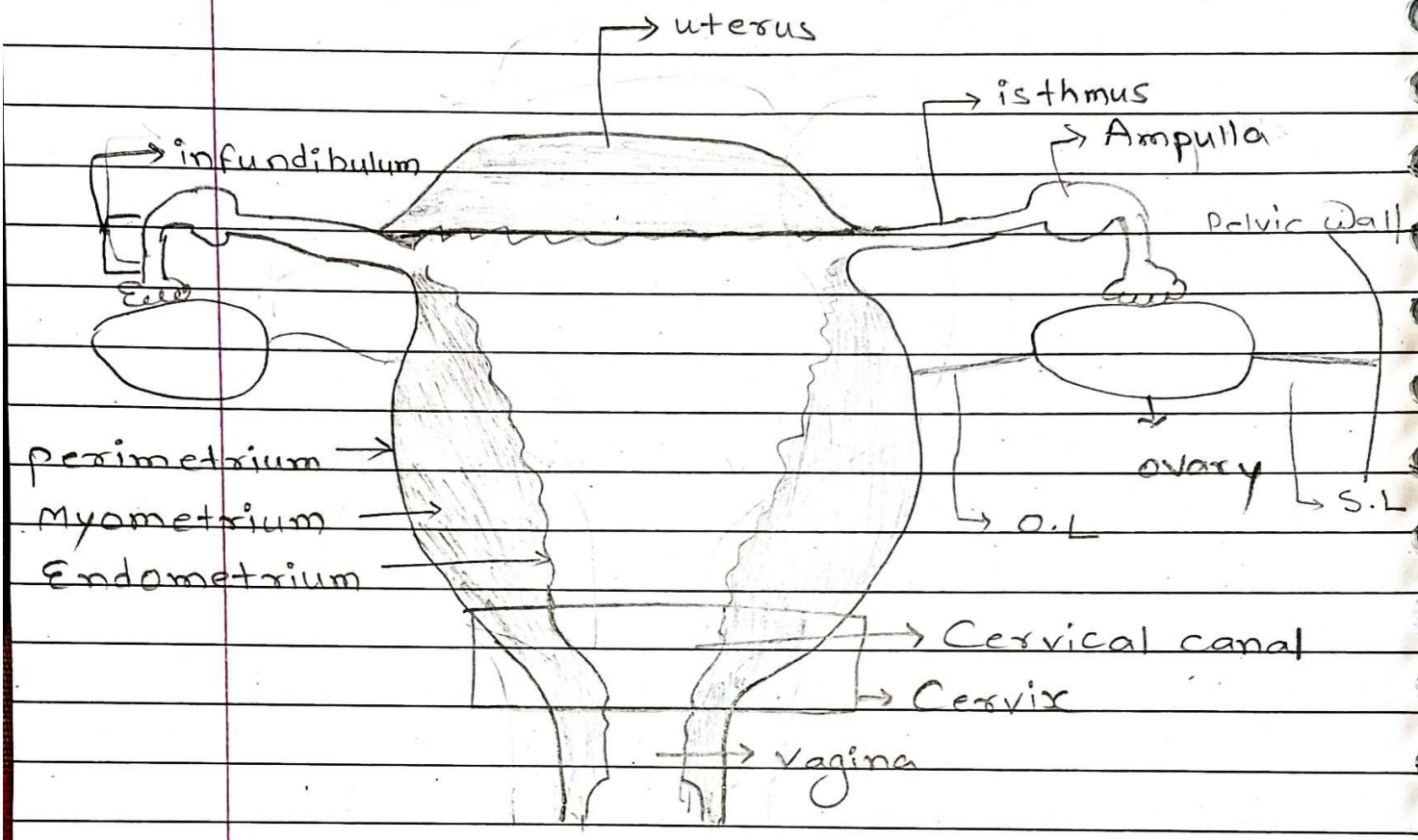

- Ovary is attached with uterine wall through ovarien ligament and with pelvic wall through suspensory ligament.

* Ovary
↳ covering = thin germinal epithelium.

- primary sex organ, One pair, ~~teth~~
- length :- 2 to 4 cm, 1° sex organ
- it produce ♀ gamete (ovum) & ovarian hormone (progesterone and estrogen)

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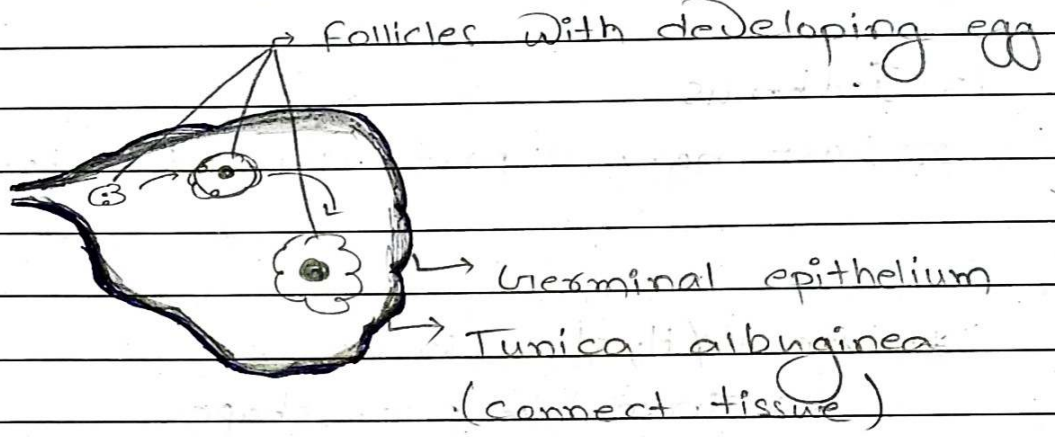
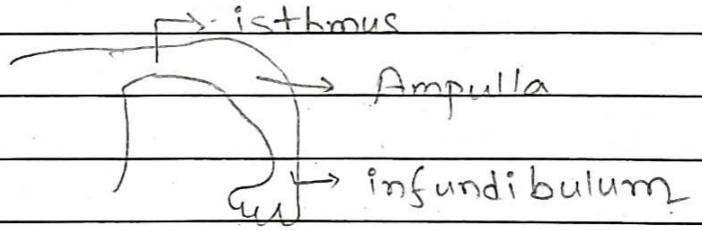
- Entire space inside ovary is called 'Stroma' & it is further divided into two parts
  (i) Cortex (outer) → has follicle
  (ii) Medulla (inner) → blood vessels



* Fallopian tube / oviduct

- Ciliated columnar epithelium
- Length = 10–12 cm



- There are three parts of oviduct.

(1) Infundibulum
→ funnel like structure
→ finger like projection emerge from infundibulum ~~fim~~ called fimbriae to collect ova.

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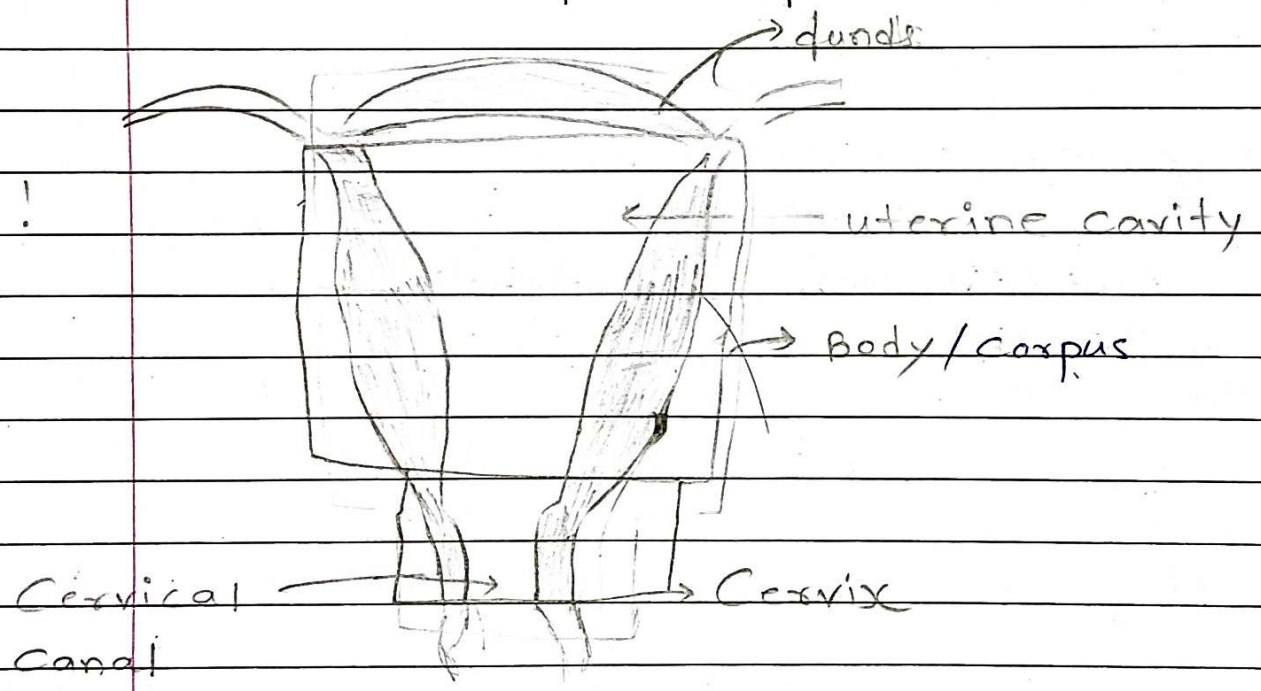
(2) Ampulla
→ Wider part of fallopian tube where fertili-sation occurs

(3) Isthmus
→ Last, narrow part, close to uterus.

* Uterus / Hystra / Womb
↳ Inverted pear shape



• parts of uterus

→ It has three parts
(i) funds
→ Top, dome shaped, where implantation occurs (specially in endometrium)

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(ii) Body
→ Middle part

(iii) Cervix
→ Last, narrow part of uterus

• Wall of uterus
→ There are three wall/layer of uterus

(i) Perimetrium (C.T + E.T, thin)
→ Outermost layer

(ii) Myometrium: (Thick)
→ Middle layer, has smooth muscles, which contracts upon action of oxytocin & help in childbirth.

(iii) Endometrium (Glandular)
→ Innermost & highly vascular
→ Undergoes maxium changes during menstrual cycle.
→ Every month, it prepares for pregnancy by thickening under influence of estrogen

→ But if pregnancy does not happen, it breaks in the form of menstrual blood.

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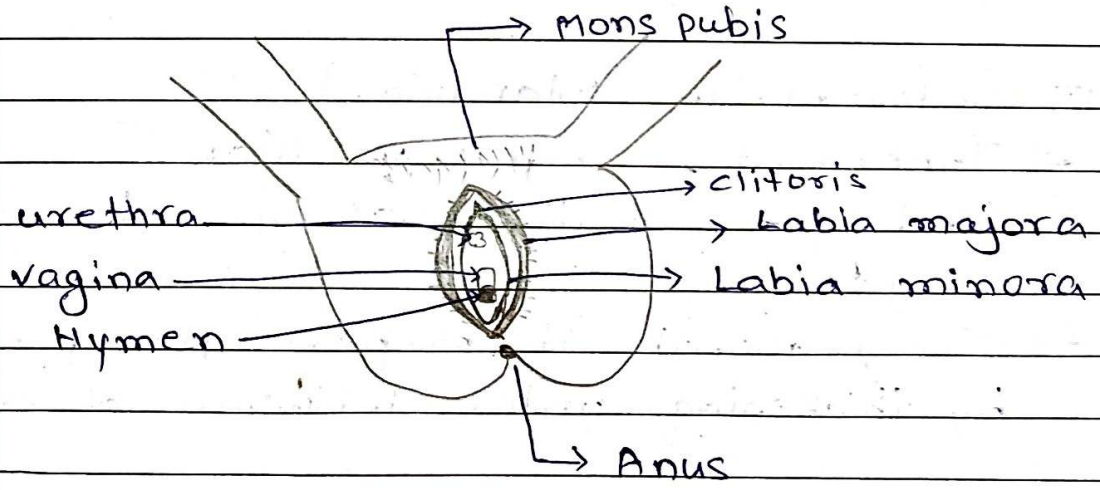
Extra

Endometrium has 2 layer :-
(i) stratum basalis (ii) stratum functionalis
. stratum functionalis break during period

* Vagina
→ This is the copulatory canal
→ Along with cervical canal it forms — Birth canal.

* Female external genitalia
→ Also known as Vulva
→ In consist of :- Mons pubis, Labia majora, Labia minora, clitoris and hymen.



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(1) Mons pubis
→ Cushion of fatty tissue covered with skin & pubic hair

→ Homologous organ with scrotum

(2) Labia majora
→ paired fold of tissue that extends from mons pubis, with pubic hair surrounds the vaginal oriffice (opening)

(3) Labia minora
→ paired & fold of tissue under majora, no pubic hair.

→ Homologous with penis

(4) Clitoris
→ Tiny ~~fig~~ fingure like structure present at the junction of 2 Labia minora just above the urethral opening.

(5) Hymen
→ Membrane that partially covers vaginal oriffice

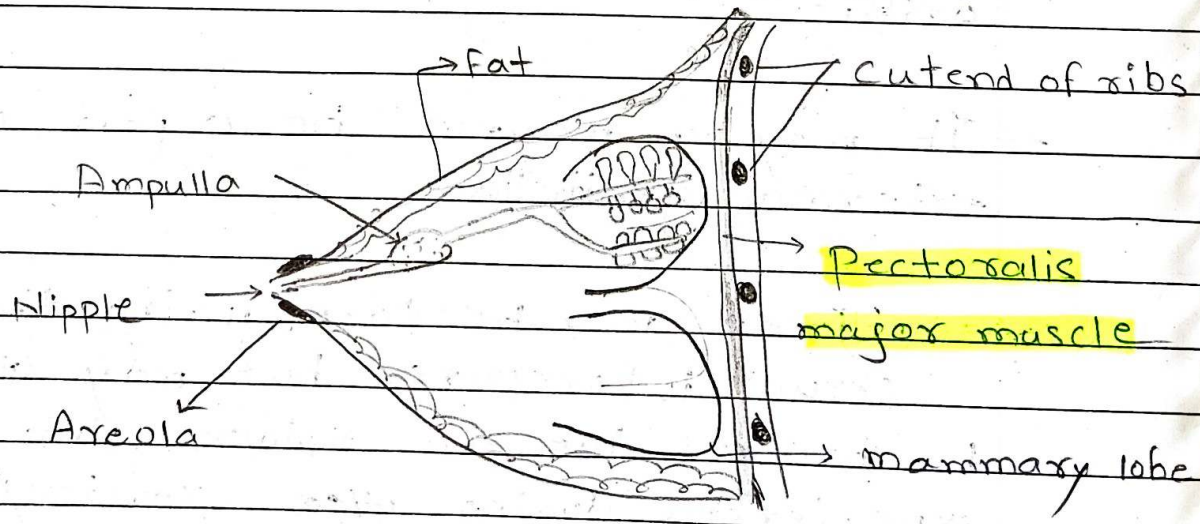
→ It may or maynot be a part of ~~f~~ external genitalia

Note :- Hymen may be torn during the 1st sexual intercourse but may also be broken due to sudden joint or fall experienced during ~~exe~~ exercise/cycling /horse riding & also due to insertion

of menstrual cup/tampons during period

* Mammary gland

- functional mammary gland is the characterstic feature of ♀ mammals
- one pair, modified sweat/sudorific gland
- Location: on pectoralis major muscle
- mammary glands has variable amount of fat & glandular tissue
- At puberty mammary gland grow under influence of estrogen.
- During pregnancy mammary gland grow under influence of prolactin, progesterone.



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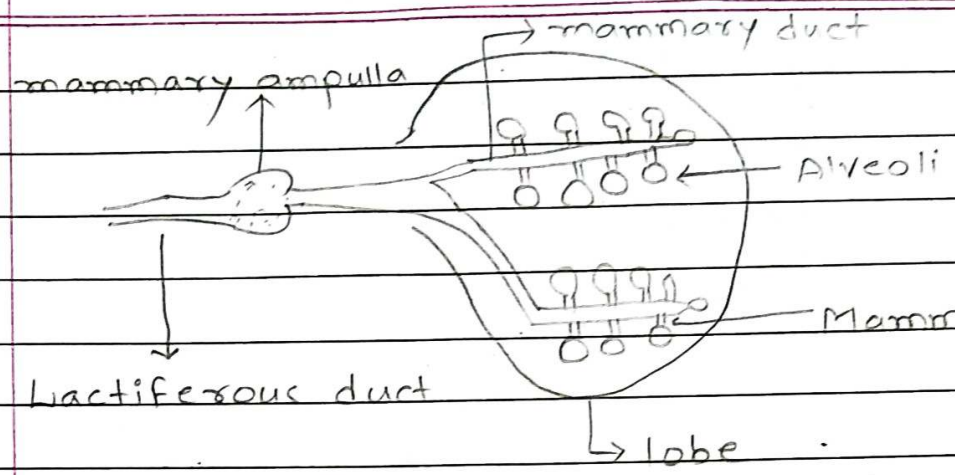

- Glandular tissue of each mammary gland is divided into :-

↓

15 - 20 mammary lobes

↓

Each lobe has ~~ex~~ clusters of milk forming structures known as mammary alveoli & also store milk.

↓

from alveoli milk carried via mammary tubule

↓

M. tubule joins to form mammary ducts

↓

M. Ducts joins to form a wider mammary ampulla.

↓

Ampulla leads to Lactiferous duct that open into nipple from where milk is sucked

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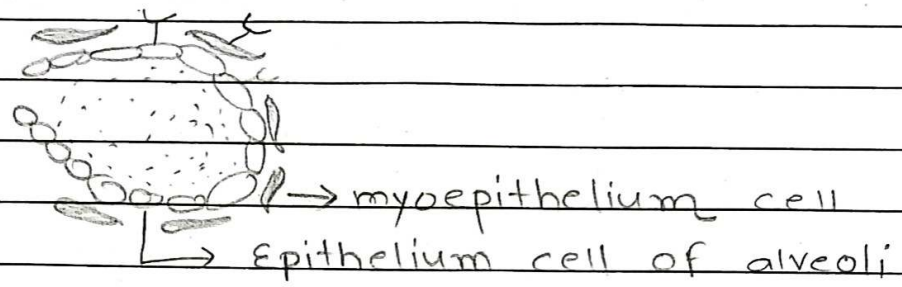
* Mammary alveoli



- Prolactin hormone acts on epithelial cell of alveoli to synthesis milk.
- Oxytocin hormone acts on myoepithelial cell to contract epithelial cells of alveoli

* Lactation

→ The process of synthesis of milk is called Lactation
→ Occur during end of pregnancy.

- The milk produced during initial few day of lactation is called Colostrum. which contains several antibodies (IgA) absolutely essential to develop resistance for new born babies

PROLACTIN

growth of mammary gland during pregnancy

Lactation

Colostrum (yellow)

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* Oogenesis

- formation of mature ova is called oogenesis
- Initiated during embryonic life
- Ends at Menopause (45–50 age)

note:- Oogenesis is markedly different from spermatogenesis.

- Oogenesis in terms of 'oocyte'

embryonic life
↳ oogonia/gamete mother cell
↓ mitosis
oogonia number increase
↓
grows enter in meiosis I, which get arrested in diplotene stage of prophase I called primary oocyte (2n)

During puberty
↳ 1° oocyte complete meiosis I & large, haploid 2° oocyte and tiny haploid 1st polar body.
↓

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2° oocyte enters in meiosis II and get arrested at metaphase II

if sperm is there meiosis II get completed which form large, haploid ova and tiny, haploid 2nd polar body

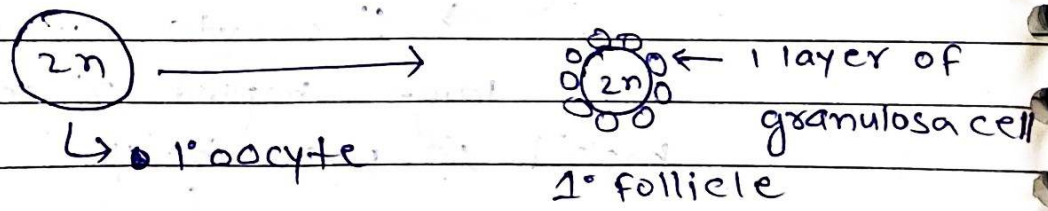
- ova & sperm fuse which cause pregnancy

If sperm is not there, meiosis II will not get completed causing bleeding phase of menstrual cycle

- Oogenesis in terms of 'Follicles'

Foetal ovary

→ 1° oocyte arrested in diplotene stage of prophase I & get surrounded by 1 layer of granulosa cell and become 1° follicle



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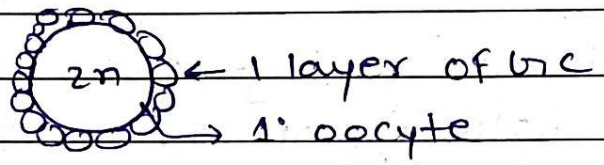
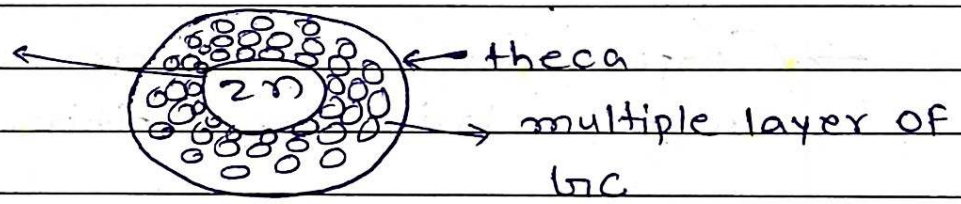
Puberty
↳ growth of follicle take place under the action of FSH

1° follicle → 2° follicle → 3° follicle → graffian/mature follicle

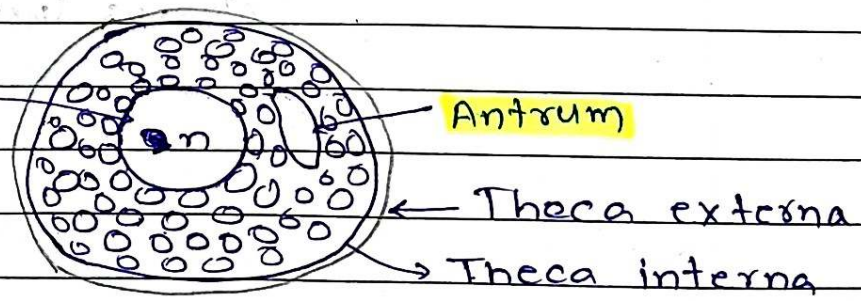
- 1° follice → 1° oocyte surrounded by 1 layer of GC



- 2° follicle → 1° oocyte surrounded by multiple layer of GC & theca layer is formed



- 3° follicle → mieosis -1 completed which lead to formation of 2° oocyte
→ Antrum (fluid - filled cavity) form
→ Theca organise into → Theca externa
↳ Theca interna



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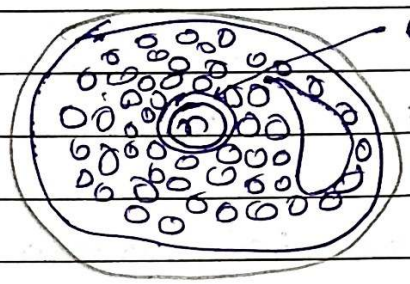
- Graffian/mature follicle

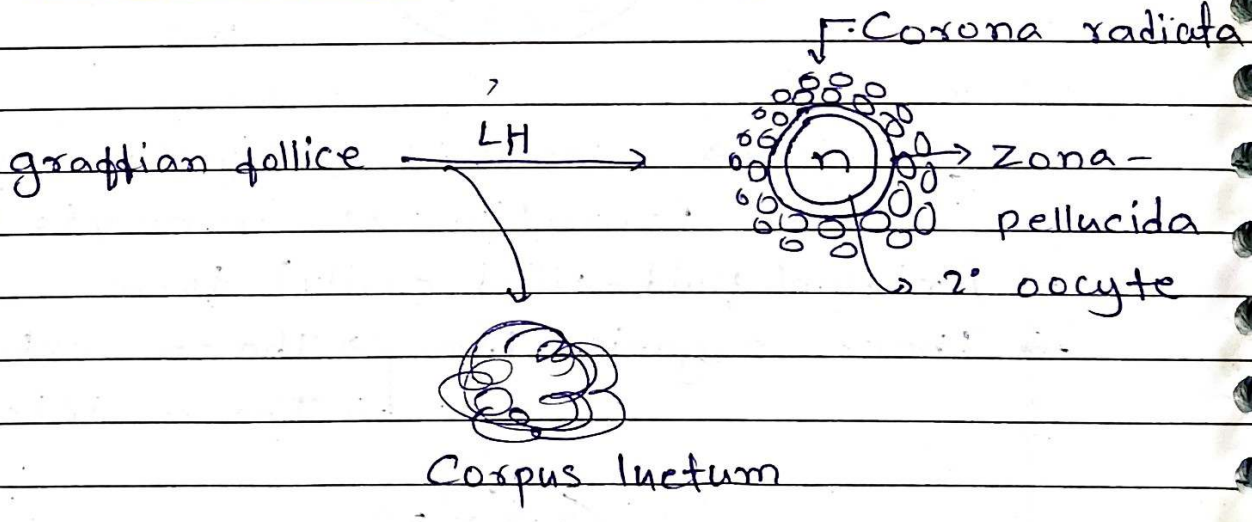
→ zona pellucida form around 2° oocyte & Antrum enlarge



→ LH acts on graffian follicle and cause rupturing of it, releasing of 2° oocyte

→ Remain ruptured part of graffian follicle form Corpus luteum (yellow body, lutein pigm)

→ Corpus luteum secrete :- Estrogen, progesterone, relaxin and inhibin.



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Note:- (i) No more oogonia are added after birth
(ii) From birth to puberty many 1' follicle - degenrate [follicular attresia]

(iii) In puberty only 60K - 80K 1' follicle are present in each ovary

(iv) In oogenesis, meiosis I and meiosis II is unequal division (in term of cytoplasm)

(v) 1 primary oocyte form 1 ova

(vi) Zona pellucida is non-cellular layer, made of Glycoprotein, Corona radiata is cellular layer (Granulosa cell)

~~(vii)~~

(vii) Meiosis I complete → in 3' follicle

(viii) meiosis II complete → after entry of sperm or before fertilisation

Secreted by oocyte & follicular cell

Note:- During the rupturing of graaffiane follicle GC gives -ve feedback to FSH. After form of corpus leteum progestrone gives -ve feedbact to LH

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- Oogenesis

Foetal ovary → oogonia
↓ mitosis
number increase
↓
oogonia grow in size and form 1° oocyte
↓

1° oocyte enters in meiosis I and get arrested at diplotene stage of prophase-I
↓
1° oocyte converted into 1° follicle

puberty → 1° follicle
↓
2° follicle
↓
3° follicle
M-I complete & 2° oocyte form
2° oocyte get arrested at metaphase II of meiosis II

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graffian follicle

rupture by LH

Corpus leuteum

2° oocyte

+ sperm
- meiosis II complete
- fertilisation & pregnancy

- sperm
- bleeding phase of menstrual cycle

* Menstrual cycle

Mammal

primate
→ ♀ primate undergo menstrual cycle

Non- primate

- Non-primate

→ ♀ non-primate undergo estrous cycle in which during breeding season, level of estrogen increase which cause sex urge & copulation

→ Estrogen cycle is suspended in non-breeding season

- Reproductive cycle of ♀ primate mammal is called Menstrual cycle. It includes events from 1 menstruation to next menstruation.

- Average menstrual cycle = 28-29 days

- Menarche → 1st menstruation (Start at puberty)

- Menopause → last menstruation (45-50 years)

- Events of Menstrual cycle is seen at :-

Ovary	Uterus
① Follicular phase	① Menstrual phase
② Ovulatory phase	② proliferative phase
③ leutal phase	③ Secretry phase

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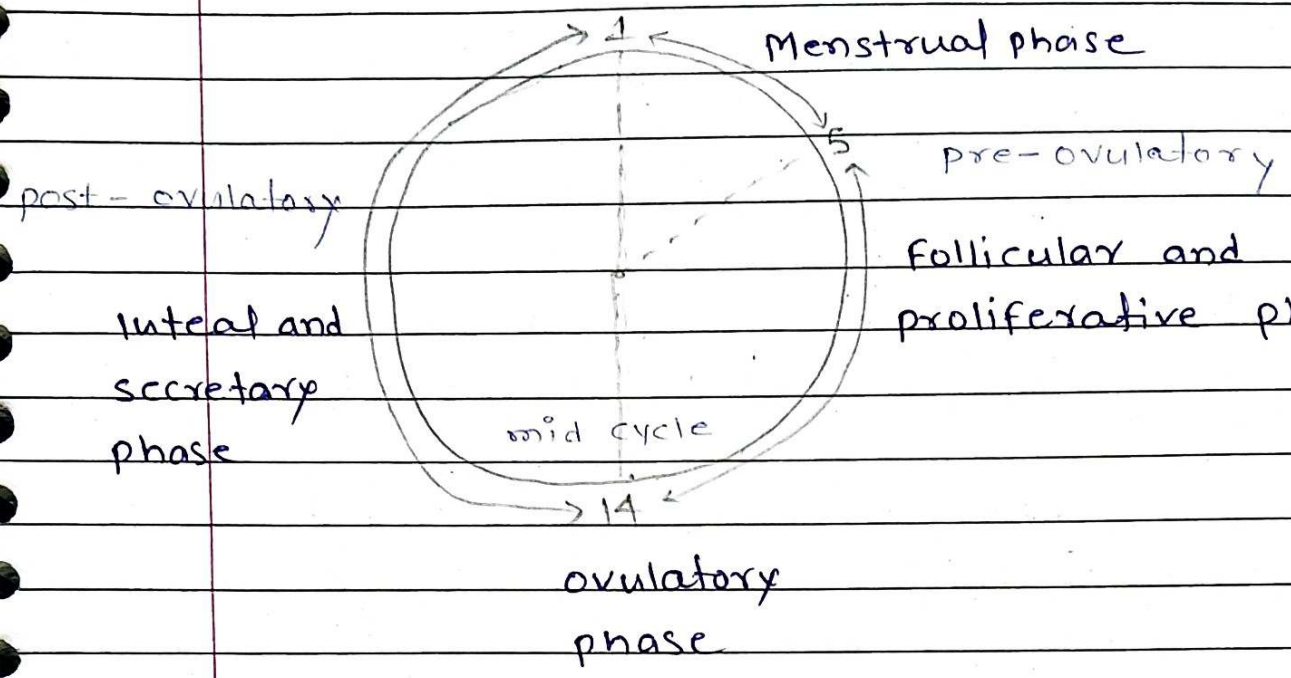

- Menstrual phase
→ Take place in uterus
→ In this phase, endometrial lining alongwith blood vessels comes out in the form of blood from vaginal opening.
→ It last for 3-5 days
→ It is also known as bleeding phase
→ Level of GnRH, LH, FSH, estrogen, progesterone is less during this phase

- follicular and proliferative phase (ovary → follicular; uterus → proliferative)

→ During this phase, GnRH increases, due to which FSH & LH also increases

→ FSH cause development of follicle

1° — 2° → 3° → Graafian follicle

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→ Growing follicle release estrogen (by GC)

→ Estrogen cause regeneration of endometrium (proliferation of endometrium)

→ At 13th day estrogen is at its peak which give +ve feedback to LH and FSH

• Luteal phase/secretory phase

→ After ovulation, ruptured graffian follicle form Corpus luetum.

→ Corpus luetum secrete → estrogen (less)
progesterone (mainly, high)
inhibin, relaxin

→ Estrogen and progestrone together give -ve feedback to LH and FSH due to which level of LH and FSH decreases in this phase

→ Estrogen & progesterone make endometrium more vascular and form glands in them which mucus and other substance.

→ life span of Corpus luetum is fixed (14 days)

→ After 14 days corpus luetum tranform into corpus albican (no progesterone is secreted)

→ As level of progesterone falls, endometrial lining again breaks and next menstrual phase begin

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Note:-

① Endometrium maintain by Progesterone

② There are two possibilities:- (After ovulation)

Sperm ✓
↓
fertilization, implantation
↓
placenta form
↓
Secrete ~~endome~~ progesterone which maintain Endometrial lining for 9 months.

Sperm ✗
↓
C.L will degenrate after 14 days, due to which progesterone level decrease which cause disintegration of Endometrium lining (Menstrual phase of next MC)

→ During pregnancy, events of MC is suspended

→ Menstrual phase occurs only if release ova is not fertilised

→ Lack of menstruation, may be an indication of pregnancy But many other factors like stress, health condition, lifestyle of a female affect her MC.

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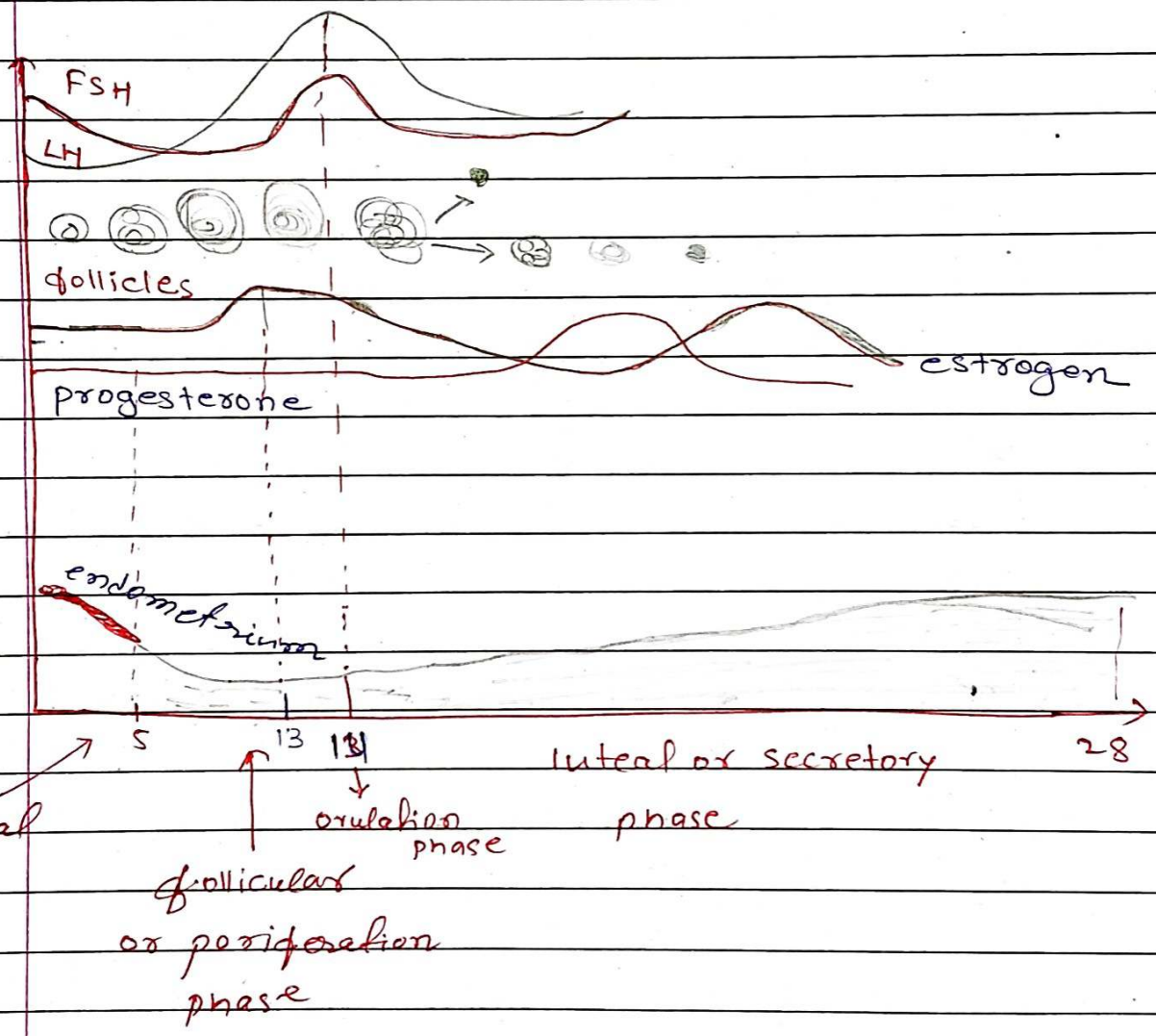
→ Hygiene is very necessary during Menstruation

→ Fixed period of event in MC ÷ Luteal phase or secretory days (14 days after ovulation)

→ Corpus luteum —Transform→ Corpus albican
yellow body — white body



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* fertilisation

- Fusion of male and female gamete to form diploid, single celled zygote is called fertilization.

- fertilization is possible only when capulation is done at the time around ovulation. So, that male and female gamete both are transported simultaneously to the ampulla of fallopian tube

- In female reproductive tract capacitation of sperm take place

- **Capacitation**

→ Capacitation is the process by which changes in sperm is made that makes the sperm able to fertilize ova

- Steps in capacitation in sperm:-

(I) removal of cholesterol layer from acrosome of sperm

(II) Dissolve decapacitation factor

(III) Entry of Ca^{2+} in sperm which cause whiplash movement of tail in sperm

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Male
↓
inseminate his sperm in vagina
↓
Capacitation of sperm occur
↓
Sperm moves from vagina to ampulla

Female
↓
Ovulation occur, releasing 2° oocyte in abdominal cavity
↓
~~reach am~~
2° oocyte enters in fimbriated infundibulum through ostium
↓
reach ampulla due to ciliated epithelium of fallopian tube

Both sperm and 2° oocyte meet at ampulla
↓
Meiosis II and fertilization occur

Q. How fertilization occur?
⇒
- Acrosomal reaction
→ Acrosome has several enzyme which help in digestion of protective layer present around 2° oocyte

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→ Due to these enzymes, pathway for entrance of sperm is formed in 2° oocyte

enzymes

- **Hyaluronidase** → digest hyaluronic acid that cement the cells of corona radiata
- **Zona lysin** → digest Zona pellucida layer
- **Corona penetrating enzyme** → Digest the cells of corona radiata

- As the sperm head touch the plasma mem. of 2° oocyte, meiosis II resume and get completed, which result in the formation of ova. Nucleus of ova and sperm fuse to form zygote

- **polyspermy**

polyspermy is a condition where single ova is fertilised by 2 or more sperms. In human, polyspermy is blocked by 2 method :-

1. **fast blockage** (temporary & fast)
2. **Slow blockage** (permanant & slow)

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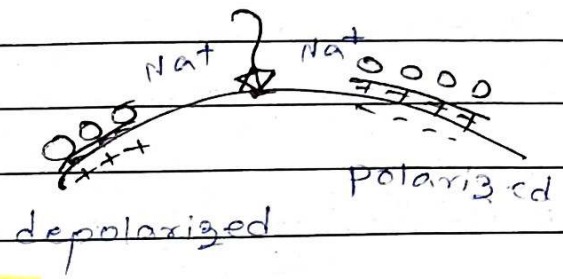
① Fast blockage



as sperm touch plasma membrane of ova

↓

Na+ channel present on surface of ova open

↓

Na+ move from outside to inside causing depolarization

↓

No more sperm can fertilize a depolarize membrane of ova

② Slow blockage

→ Due to depolarization of plasma membrane of 2° oocyte, Ca^{2+} level in cytoplasm increases.

→ Ca^{2+} will cause exocytosis of cortical granules (present in cytoplasm) (cortical reaction)

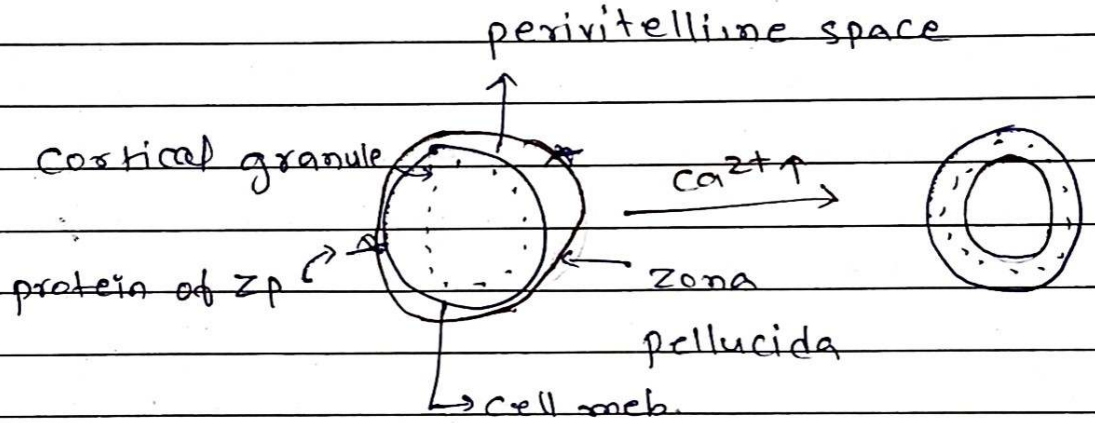
→ Cortical granules enter in perivitelline space and cause :-

(i) Destruction of protein present on Zona pellucida (Zona reaction)

(ii) Hardening of zona pellucida

→ Due to hardening of zona pellucida, no more sperm can enter in 2° oocyte

→ It is permanant in nature



• Cleavage

→ Rapid mitotic division
→ cell skip growth phase
→ Each cell get equal amount of DNA (2n) but cytoplasmic content decreases.
→ As zygote moves towards uterus, cleavage proceeds

Zygote → 2 cell — 4 — 8 — 16 cell → Blastocyst or Blastula

Morula

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→ Gastrula

- Blastocyst get implanted in the endometrium of uterus

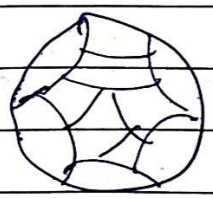
- Morula
→ Solid ball like structure
→ Mulberry like
→ No cavity

- Blastula/ Blastocyst
→ hollow ball like
→ cell arranged in → outer layer (trophoblast)
→ inner cell mass
→ blastocoel cavity present

- Gastrula (Gastrulation occurs)
→ formation of 3 germ layers occur ÷
Ectoderm, Endoderm, mesoderm

- Trophoblast of Blastula will help in implantation and placenta formation.

- ICM will participate in formation of embryo



Morula

Blastocyst

Stem cells

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* Implantation

→ Blastula get attatched to the endometrium of uterus
→ Uterine tissue also divides and cover the blastula. Due to which blastula get embedded in the endometrium of uterus.

→ Implantation leads to pregnancy

* Placenta formation

→ After implantation, finger like projections arise from trophoblast called Chorionic villi which become interdigitated with the mother's uterine tissue and form structural & functional connection b/w mother and developing embryo called placenta

- Functions of placenta :-

(i) Provide O_2 and nutrients (→ antibiotic) to developing embryo
(ii) Remove CO_2 and excretory waste from developing embryo.
(iii) Act as temporary Endocrine body (release hormone :- HCG, HPL, estrogen, progesterone)

(iv) Act as barrier so that Maternal and foetal blood cannot get mixed.

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→ contain artery & vein

→ Umbilical cords connects placenta and growing foetus.

→ During pregnancy, hormones like estrogen, progestrone, thyroxine, cortisol etc increases several fold in the mother's blood for the normal development of the fetus and Healthy mother.

• Hormone by placenta :-

① HCG (Human chorionic gonadotrophin)

→ maintain Corpus luteum, acts as LH
→ Detected during pregnancy test in urine of female.

② HPL (Human placental lactogen)

→ prepare mammary gland for lactation.

③ CRF (Corticotrophic releasing factor)

→ Act on adrenal cortex and cause release of cortisol.

Note :- HCG, HPL and relaxin are produced only during pregancy.

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(4) Estrogen & Progestrone

→ Maintain endometrium
→ Development of mammary gland.

* Organogenesis
→ form of organs.

Week
Month
Trimester

- End of 1st month → Heart
- " " 2nd " → limbs, digit
- " " 3rd month/1st trimester → major organ system + external genitals
- End of 5th month → 1st movement, hairs on head
- End of 6th month/2nd trimester → Hair on body, eyelase formed, eyelids seprate
- End of 9th month/3rd trimester → fully developed foetus is ready for parturition

* Parturition (complex neuro-endocrine mechanism)

fully developed foetus & placenta
↳
{ signal

foetal ejection reflex
↓

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Uterus muscle contract

↓

Signal to mother's hypothalamus, ~~fuel~~ further signal to Neurohypophysis / posterior pituitary

↓

posterior pituitary release oxytocin (birth hormone)

↓

Strong uterine contraction

↓

parturition / Child ~~det~~ delivery

→ After delivery of child, placenta is also expelled out

→ Relaxin is release in later phase of pregnancy

- → by ovary !
- → Relax pubic symphysis (aid in child birth)

Note :- Labor can induced by administering pitocin

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Twin

Monozygotic twins
↳ identical twin

Dizygotic twins
↳ Non-identical twin

* Lactation

Hypothalmus :- PRH , PIH

PRH ↓ acts on anterior pitutary ↓ prolaction

PIH ↓ acts on anterior pitutary ↓ Stop secretion of prolaction

prolaction → growth of breasts during pregnancy

prolaction → Lactation

note • During the pregnancy other hormone like estrogens, progestogens, cortisol, prolactin, thyroxine etc are increased severalfolds in maternal blood.

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- Gastrula
  ↳ Early state of embryo, has an opening called blastopore
- Gastrulation
  ↳ formation of germ layers of embryo is called gastrulation.
- Cells of Rauber (chorion & amnion) & Allantois
  ↳ Connect Trophoblast & inner mass cells
- Chorionic gonadotropin

Evolution

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* Introduction

- Evolutionary Biology is the study of past of life forms present on Earth.
- Changes in flora and fauna that have occured over millions years, is known as evolution.
- Evolution is slow and continous process.
- Evolution mean to unfold or unroll.
- We will study :- orgin of universe.
  orgin of Earth
  orgin of life.

Case :- When we're looking at star, actually we are peping into the past

Reason :- Stars are trillions of kilometer far from us. Light reflected from stars take millions of years to reach our eyes. Hence, what we are looking today, is actually the position of star million of years ago.

- Stellar distance are measured in light years.

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* Origin of Universe

- Origin of universe = 20BYA
- Origin of universe explaind by BIG BANG theory (by Abbe lemaitre)
- Big bang theory :- single huge massive explosion
  → unimaginable in physical term

Single entity
↓ explosion
many nebulas form
tem. cool down
Hydrogen, Helium formed later
↓
stars, clouds of gases and dust condensed under gravity and form galaxies
↓
Many galaxies formed, one of them is our galaxy (milky way or Akash ganga)
↓
In our galaxy, there is solar system which includes our planet, Earth
↳ Formed 4.5BYA

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- Early earth has no atmosphere
-
- Volcanic eruptions occur which releases H_2O vapour, CO_2, NH_3, CH_4
- No ozone was there, UV light easily present on earth.

$$H_2O \xrightarrow{UV} H_2 + O_2$$

H_2 → lighter gas → escaped

O_2 → reactive → react with other gases.

- When atmosphere formed it was reducing type → no free O_2 found
- Also, there was rain for many years, which filled the depression on earth and formed Oceans.
- Life originated in water about 500 million year after formation of Earth (i.e 4BYA)

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* Origin of life.

Many theories are given to explain the origin of life on earth.

(1) Theory of special creation.

→ A/c to this theory, life was created by God.

→ Different religion literature explain it in different ways.

→ Support of Father Saurez.

→ A/c to this theory, age of Earth is 400 years.

→ Diversity in ~~am~~ animals is same as early earth and will be same in future.

→ No scientific proof, this theory was discarded.

(2) Theory of panspermia

- Also known as theory of extra-terrestrial life or cosmozoic theory

- A/c to this theory, life come from different planet on Earth in the form of Spores (unit of life)

- Early greek thinker believed this theory

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- Given by Arrhenius

- ~~may~~ Many astronomers still ~~betie~~ belive this theory.

(3) Theory of Abiogenesis

- Also known as theory of spontenuse generation

- Abiogenesis → life from non-living thing
  - not
  - life
  - formation

- A/c to this theory, life arise spontenousely from non-living matter like - straw, mud etc.

e.g. mice spontenusly formed in the dark room filled with straw.

- This theory disproved by experiment done by Louis Pasteur.

(4) Theory of Biogenesis

- A/c to this theory, life came form pre-existing life.

- Biogenesis
  - life
  - formation.

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- Demerit :- This theory doesn't explain how 1st life originated on Earth.

- Louis Posteur, Redi, Spllanzani are 3 scientists who work on providing life comes from pre-existing life.

- Louis Posteur performed Swan Nect experiment.
  - ↳ Disproved theory of Abiogenesis
  - ↳ proved theory of Biogenesis

- Swan-nect experiment

Case I. pre-steriti swan-neck shape flask

↓

prepare broth (nutritive-medium)
H_2O + sugar + killed yeast

↓

Boil it

↓

No growth of bacteria from killed yeast or rotting material

Conclusion :- Theory of Abiogenesis disproved

note :- Air from outside get trapped in the swan neck of flask.

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Case II Same as case I, but break swan-nick of flask

Air can easily enter in the flask. Air have micro-organism which successfully grow in broth

Growth of micro-organism seen.

Conclusion:- life came from pre-existing life (New micro-organism from pre-existing micro organism)

Theory of Biogenesis is proved

(5) Theory of chemical evolution or chemogeny

- Given by Oparin (Rusia) and Haldane (England)
- Also known as Oparin-Haldane's theory
- A/c to this theory, 1st life was created from non-living organic molecule.
- free atom → inorganic molecule → Simple organic molecule → complex organic molecule → formation of coacervate or microsphere

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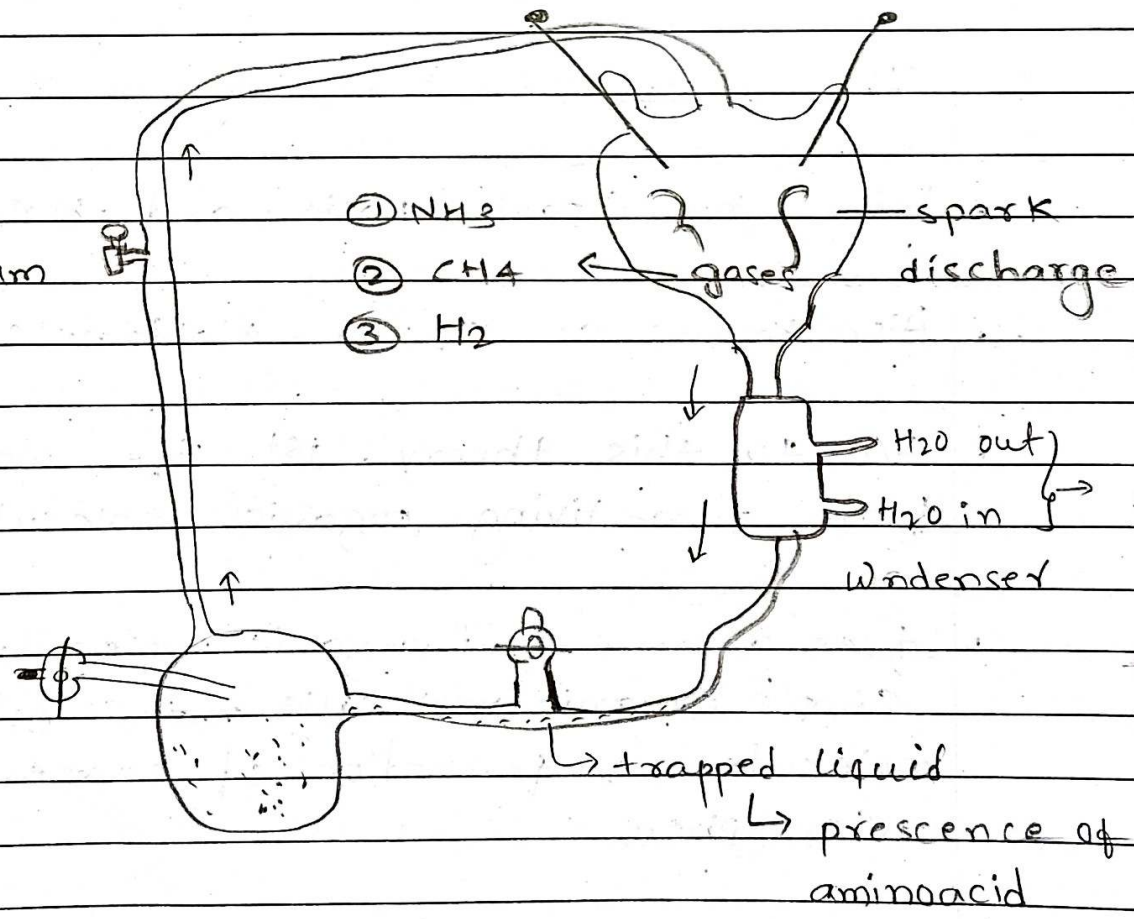
note:- Microsphere & coacervates are also known as protobiants.

- Condition of perimitive Earth:-
High tem., volcanic storm, Reducing atmosphere, atmosphere containing CH_4, NH_3, H_2 etc

- Chemical evolution was proposed by Haldane & Oparin but was experimentally proven by Miller & Urey (1953)

- Miller & Urey replicated the environment of primitive Earth in lab and proved theory of chemical Evolution.



Experimental setup of Miller's experiment

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* Miller's experiment

- Spark discharge experiment
- In the chamber, 3 gases were taken ($CH_4 : NH_3 : H_2$ 2 : 1 : 2)
- Electrodes (tungsten) produce 75000 voltage
- Temperature = 800°C
- After 15 days, he observed formation of amino acid (Glycine, Alanine, Aspartic acid)
- Similar experiments were conducted by different scientists. And they also observed formation of sugar, nitrogen base, fat etc.

- Origin of universe ÷ 20BYA OR 13.8BYA
  Origin of Earth ÷ 4.5 BYA
  Origin of life ÷ 4BYA
  Origin of non-cellular life (RNA, protein) ÷ 3BYA
  Origin of cellular life ÷ 2BYA

* Sequence of evolution

Chemohecterotroph

↓

Chemoautotrophs

↓

Anaerobic photoautotroph

↓

Aerobic photoautotroph

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Note:- Initially autotroph use H_2S. later autotroph use H_2O.

Biological evolution

↳ induce by Chemical evolⁿ

- It explain the diversity present on earth.

(1) Lamarckism

- Lamark was a french naturalist. He publish his book philosphie zoologique in 1809

- Key concept of lamarckism:-

(i) Presence of internal vital force in all organism
↳ with this force all organism have the capability to make changes in organ or body

(ii) Effect of environment and new need
↳ Change in environment cause new need which further make changes in organs.

(iii) Use and disuse of organ
↳ more use of organ → more development
↳ no use of organ → start degenerating.

(iv) Inheritance of acquired characters
→ Acquired characters are those which are gained in lifetime.

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- A/c to lamarckism, acquired characters are inherited in further generation.

- e.g of lamarckism → long neck and limbs of giraffe.
  → limbless snake

Note :- Presence of vestigial organ support this theory

- This theory is also known as 'Theory of use & disuse of organ' or Theory of inheritance of acquired character.

(2) Theory of continuity of germplasm

Our body has
- Somatic cell
- Germ cell → gamete

- This theory was given by August Weismann

- A/c to this theory, only those changes are inherited in future generations which are occured in germ cell

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- Experiment done by Weismann
  ↳ cut tail of rat for 22 generation, still never tailless rat was born.

- Conclusion of experiment :- Cutting of tail is not affecting germ cell, hence this character is not inherited.

(3) Neo lamarckism
new ↳ theory of lamarck

→ Many scientists redefined Lamarckism and give Neo - Lamarckism.

→ A/c to this theory :-

Change in environment
↓
~~chage~~ change in organism that affects its germ cell
↓
Change in germ cell is inherited in future generations.

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(4) Darwinism

Charles Darwin (born in 1809)

HMS Beagle ship

Went for sea vouge for 5 years

Visited many islands, countries, but Galapgo's island was the study centre.

- Galapgos island ÷ Collection of 22 islands
  ÷ in Pacific ocean
  ÷ located at western coast of south America

- Alfred Wallance

Went on vouge and visit Malay Archipelago
↳ located in Indian ocean
↳ Now, there is Malaysia and Indonesia

- Both scientists jointly proposed Theory of Natural Selection

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- Both scientists were influenced by Eassy on population written by Thomas Mathus.

- Both scientists concluded similar observation from studies during their vouge.

- Key concept of Theory of Natural Selection

(a) Overproduction
→ Organism reproduce at maximal reproduction, at geometric ratio.

→ Differential reproduction take place
↳ Different organism give birth to different number of offspring.

(b) Struggle for existence
→ population of organism increased. But resources are limited, as a result, there is struggle for existance.

- 3 types of struggle :-

(i) Intraspecific struggle
→ Members of same species competes for basis neccessity.

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(ii) Interspecific struggle
→ Members of different species struggle for basic neccessity.

(iii) Environmental struggle
→ Struggle against extreme environmental condition like heat, cold, flood etc.

(c) Variation and heredity
→ No two individuals are same (except :- Mono-zygotic twins)
→ Variations exsist in population
→ variation → useful → selected by nature
→ NOt useful

(d) Survival of the fittest
→ Individuals with great ~~fittest~~ fitness will survive and get selected by nature
→ Darwin talks about Reproductive fitness (leave more progeney)
→ Survival of fittest idea given by Herbert Spencer

(e) Origin of New species
→ With generations, variation will get accumulate-d, and after many years new species is originated.

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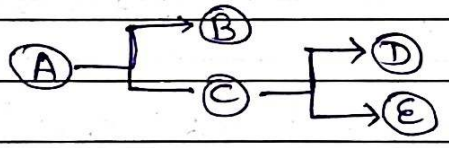
Note:- A/c to Darwin, variations are :- small, continous and have directions

. 2 key concept of Darwin

Nature selection	Branching descent
→ Gives idea ~~of~~ about mechanism of evolution	→ Gives idea about pattern of evolution → Explain common ancestor of organism



Change in DNA sequence

(5) Mutation theory

→ Given by Hugo de Vries

→ He worked on Evening primrose (Oenothera - lamarckiana)

→ A/c to this theory, Evolution has take place due to Mutation

→ A/c to Vries, Mutation are :- large change, discontinous and random or directionless.

→ This theory is also known as 'Saltation theory' (large change in one step)

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- Example of natural selection

(i) Industrial Melanism
→ In England
→ Observed on population of peppered Moth

Moth

White winged
Biston betullaria

Dark winged
Biston carbonaria

→ Lichen is a ~~pop~~ 'pollution indicater'
pollution present – lichen absent
pollution absent – lichen present

Industrial revolution

Before Industrialisation
↓
No pollution
↓
lichen present
↓

After Industrialisation
pollution present
↓
lichen absent
↓
bark of tree become
due to absence of lichen &

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give white appearance to bark of tree

presence of soot, smoke etc.

→ White winged moth blended with background

→ Dark winged moth blended with background

· Conclusion :-

→ Before Industrialisation

dark winged moth < white winged moth

→ After Industrialisation

Dark winged moth > white winged moth

(ii) Antibiotic Resistance

· Antibiotic :- Chemical that act against bacteria or kill bacteria

· After use of antibiotic, some bacteria become resistant to that chemical, which means bacteria will grow even in the presence of that chemical. This property is known as Antibiotic Resistance.

e.g. Selection of bacteria with specific antibiotic resistance

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(6) Neo-Darwinism

→ Also known as Modern synthetic theory of evolution

→ Darwinism + Mendelion genetics

→ Explain arrival of fittest, source of variation

Note:- unit of evolution - population
unit of natural selection - individual

- Source of variation
(a) Migration (b) Genetic Recombination
(c) Mutation (d) Genetic Drift (e) Natural selection

* Migration or Gene flow

- Movement of individuals from one place to another
- Migration result in Gene flow
- Migration
  - → Emmigration (exist or out)
  - → Immigration (in or entery)

* Genetic Recombination

- During cell division, crossing over takes place
- ~~Resultting~~ Resulting in exchange of section of chromosome among chromosome
- Source of variation

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* Mutation

- Change in base pair in a polynucleotide chain (DNA)
- Source of variation
- Random and directionless in nature

* Natural selection

- Nature selects individual with +ve variation and support fittest.

- Types of Natural selection

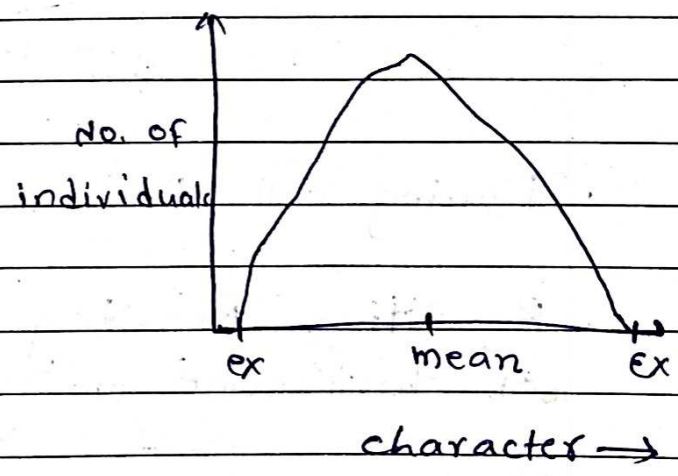
(a) Stabilising selection

→ In this, individuals with mean/average/intermediate characters are selected.

→ Individuals with extreme characters are eliminated

→ It indicates unchanged/constant environment

→ e.g. height of individual



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→ With time peak gets narrower and longer

(b) Directional / progressive selection

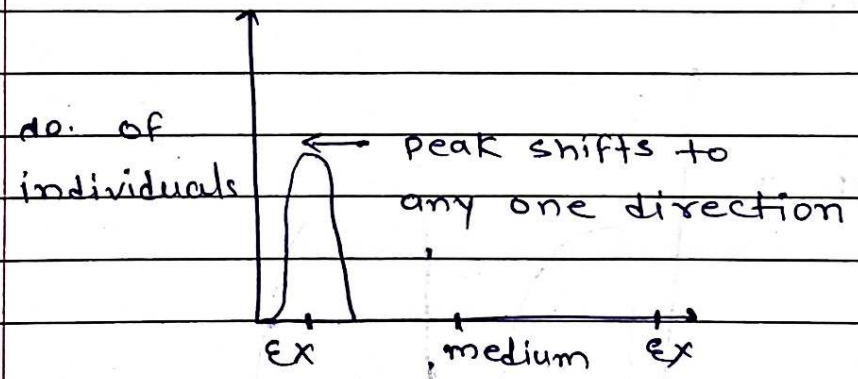
→ In this the peak shifts to any one extreme character

→ Nature selects any one ~~the~~ peripheral character at a time.

e.g. Industrial melanism

Before industrialisation white winged moth get selected

After industrialisation Dark winged moth get selected.



(c) Disruptive selection

→ In this, nature selects both extreme character at the same time

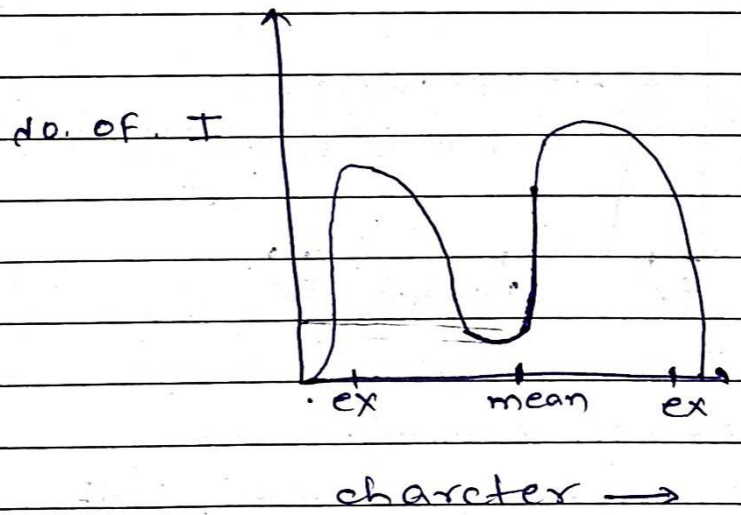
→ Mean character is not favoured by nature

→ 2 peaks are found in this type of selection

→ e.g. Mollusca/ ~~sait~~ snail have 3 color of cell

Black (extreme trait)	Grey (medium trait)	White (extreme trait)
↓	↓	↓
blend with color of rock	eaten by predator	blend with sand

Conculsion ÷ Nature selects both extreme character at the same time, Not medium character.



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* Genetic Drift

- Change in allelic frequency due to by chance factor
- Random in nature
- Its impact is seen in small population
- Also known as Sewall wright effect or Scattering of Variability

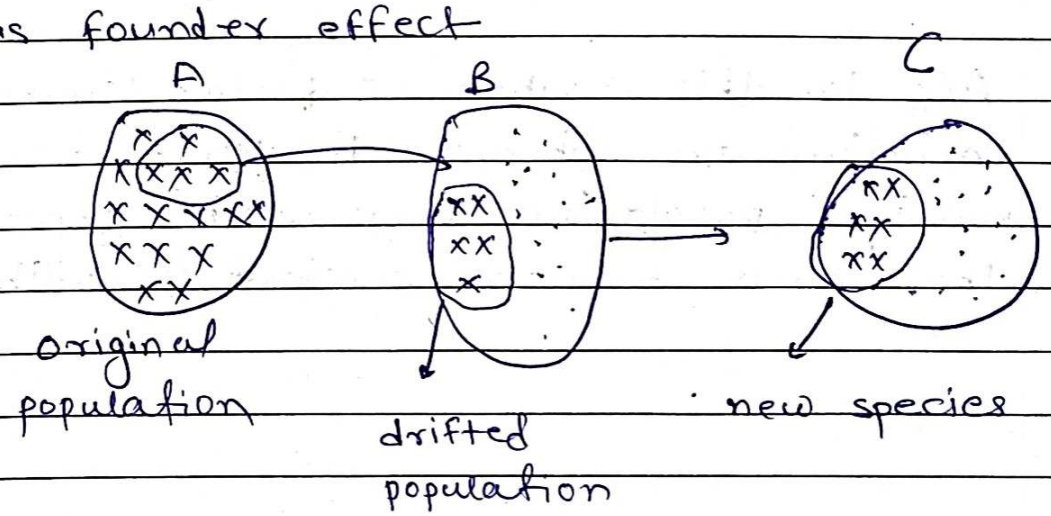
Genetic Drift result in

- Founder effect
- Bottleneck effect

- Founder effect

When drifted population give rise to new species in a new geographical isolated location

→ It means Drifted population become the founder of new species. This effect is known as founder effect



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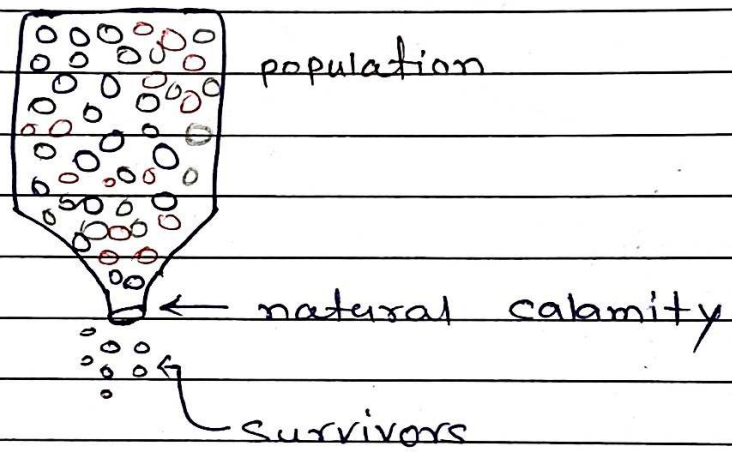
- Bottleneck effect

→ Random change in allelic frequency in a population due to natural calamities.

→ This cause loss of genes and loss of traits

→ Survivors mate & regain population size and may form new species in future



* Hardy Weinberg Equilibrium

- Given by Hardy & Weinberg

- A/c to this, when 5 factor (source of variation) are absent in large, random mating population then the gene pool of the area remain constant (Equilibrium)

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- 5 factors affecting Hardy - Weinberg equilibrium are :- Mutation, Migration, Genetic Recombination, Natural selection & Genetic Drift

- Gene pool → Sum of all gene & its alleles.

- Hardy - Weinberg Equation

$$p + q = 1$$

p = frequency of dominant allele
q = " " recessive allele

$$p^2 + q^2 + 2pq = 1$$

p^2 = frequency of homozygous dominant condition

q^2 = frequency of homozygous recessive condition

pq = frequency of heterozygous condition

Q. Frequency of A = 0.7
frequency of a = 1 - 0.7 = 0.3

Q. Total polution = 1000
AA = 360
Aa = 480
aa = 160

Find frequency of A :- $360 + \frac{480}{2} \rightarrow \frac{600}{1000} = 0.6$

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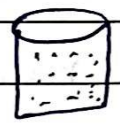
Q. Frequency of A = 0.4
find AA, Aa, aa

→ $AA = (0.4)^2 \rightarrow 0.16$
$Aa = 2 \times 0.4 \times 0.6 = 0.48$
& $aa = (0.6)^2 = 0.36$
add = 1

* Lederberg's experiment

- Done by Lederberg scientist
- Experiment :-



bacterias growing in medium A over several generation

Medium A

↓

bacterias tranfered from medium A to medium B

Medium B
(contain penicillin)
↳ Antibiotic

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Result ÷ Only few bacteria survived in MediumB. Only those bacteria survived which were having pre-existing advantageous mutation (Resistance against pencillin)

* Isolation

- When member of same species become seprated from original population due to any reason

for.e.g. formation of moutain (physical barrier that member of population can't cross)

* Reproductive isolation

- Isolation due to reproductive reason (some members of same species is not able to reproduce with original population)

Reproductive isolation

pre-zygotic

→ No fertilisation
→ No formation of zygote

post-zygotic

→ Formation of steril organism

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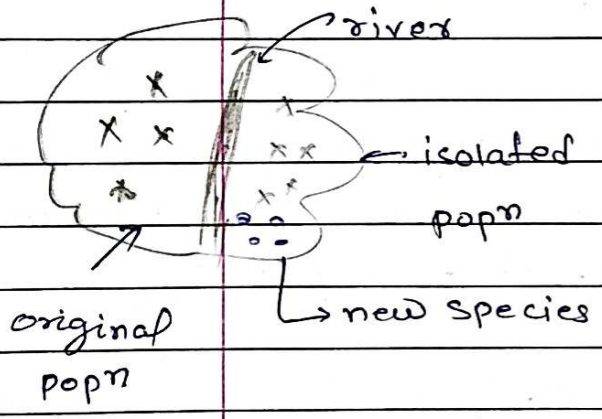
* Speciation

- formation of new species is known as speciation.

Speciation

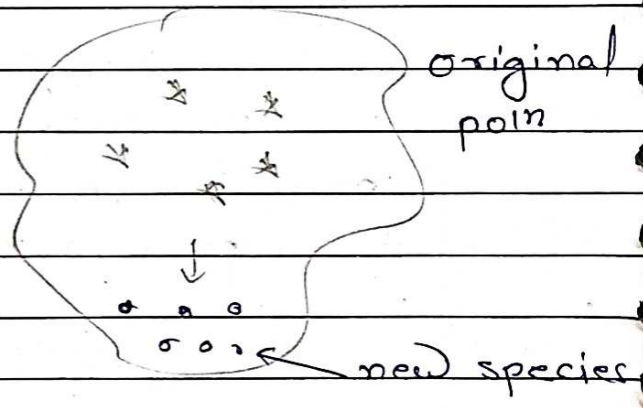
Allopatric

→ formation of new species due to geographical isolation



Sympatric

→ formation of new species in the same population at the same geographical location.



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* Evidences for evolution

(1) Fossils

→ Study of fossils is known as palaeontology

Palaeontology

Palaebotany → Study of plant fossils

Palaeozoology → Study of animal fossils

→ Fossils are remains of hard parts of life forms found in rock

→ Generally found in Sedimentary rock

→ e.g of fossils :- imprints, excreta, bones etc.

• Age of fossis

↳ Dertermined by :-

(a) Carbon Dating method

→ Isotopes of carbon is analyse

→ ratio of different isotops of carbon is used to know the age of fossils

ex. of living fossils :- Amphioxus, Varanus, Lamprey

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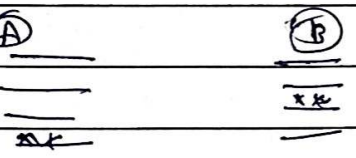
(b) ESR (electron spin resonance)
→ recent technique
→ give accurate result

(c) Relative method
→ fossils found near the surface of earth is recent while fossils found in deep layers of earth is comparitively older

e.g. (A) (B)



(B) is recent in comparison to A

(2) Morphological and Anatomical evidence

- Homologous Organ

↳ Same origin
Same ancestor but different function
Same structure

→ Homologous organs indicate common ancestor
→ Due to different environment, different needs

↓

Same structure perform different function

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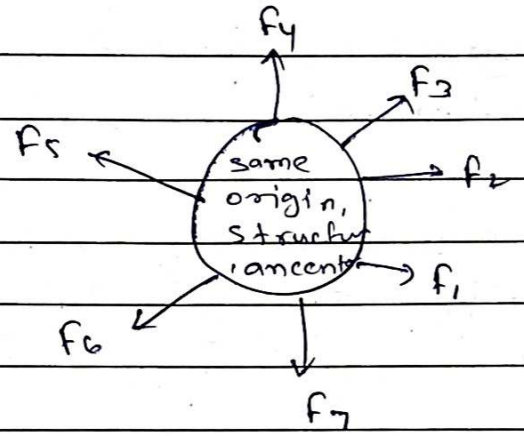
→ Homologous organ is also known as :-
Divergent evolution



f_1 — f_2 are different function

e.g. ⓐ ~~four~~ forelimbs of cheetah (run), whale (swim), bat (fly), human (lift obj)
(same structures - humerus, radius, ulna etc)
(different function)

ⓑ Thorn of bougainvilea and tendril (support) of cucur-bita
defense
(both arise from axillary bud, different funcn)

ⓒ Hearts and brains of vertebrates

ⓓ Mouth parts of cockroach, honeybee, mosquito
(same structure maxillae, mandible, function different)

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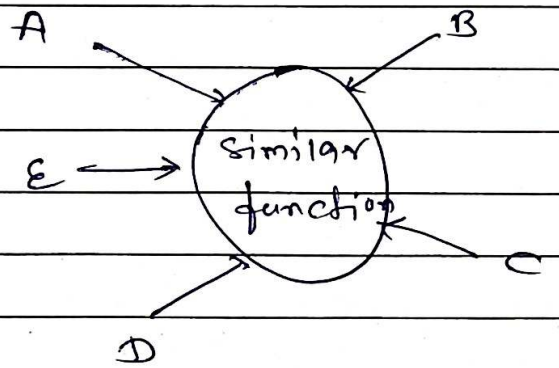
- Analogus Organ

→ Different ancenter
Different orgin but Similar fuction
Different Structure

→ This happens due to some environment, some needs of different organ living in similar conditions.

→ Analogus organ indicates different ancentory.

→ Analogus organ indicates Convergent evolution



e.g. ⓐ potato and sweet potato
(stem modification) (root modification)
→ both store food

ⓑ Wings of butterfly and birds

ⓒ Eye of octopus and human.

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(d) flippers of penguin and dolphain

(3) Biochemical Evidences

→ On the basis of similarities in genes and protein found in different animals indicates common acestory

e.g. Trypsin enzyme

(4) Vesitigial organ

→ Vesitiginal organs are those organs which are present in reduced form and non-functional form now. But they are functional in acentor and animals having common ancestor.

e.g of vesitiginal organs in human

- nipples in male
- body hair
- third molar (wisdom tooth)
- Muscle of ear pinna
- oppendix
- Tail bone (coccyx)

date ÷ Atavism

↳ Reocarrence of ancentral trait

e.g. presence of tail in new born

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(5) Biogenetic Law/embryological evidences

→ Given by
→ A/c to him embryo of all higher vertebrates have certain characters that is absent in adult form. e.g. gill slit is present in human embryo ~~that is absent in adult human~~

* Adaptive radiation

Adaptation — radiating in different dirn

→ When members from original population in a geographical location move to different geographical location. Then due to different location some changes occur in them. Due to which many varities (species) are formed. This is known as Adaptive radiation

→ It is Divergent evolution

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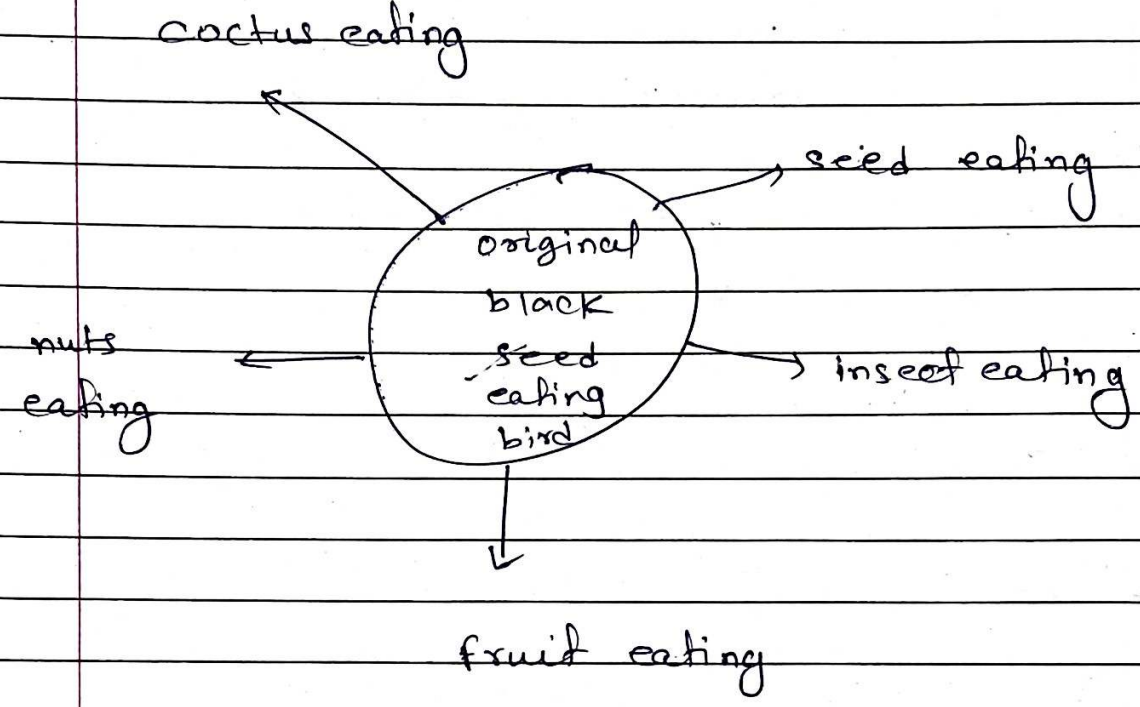
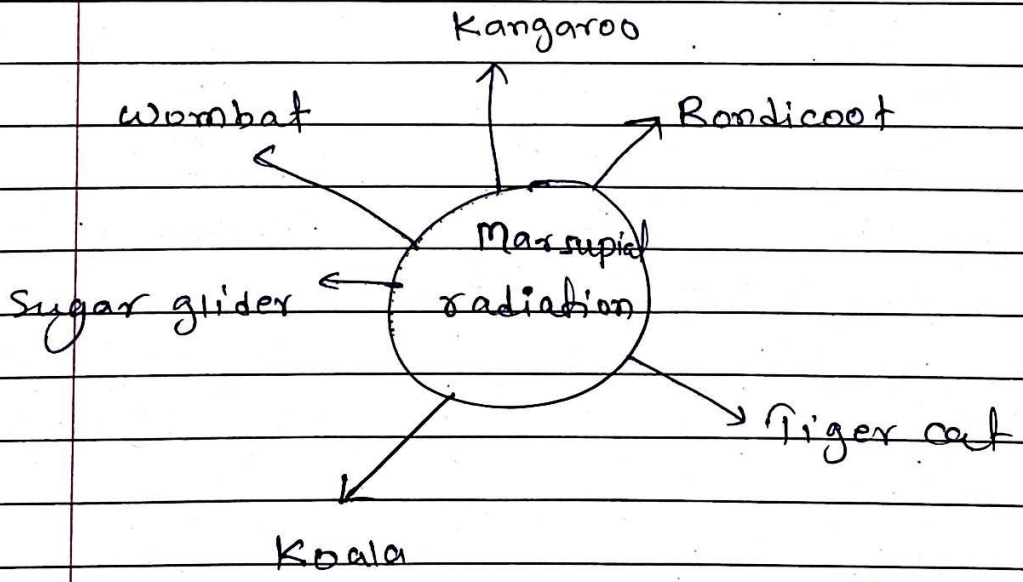
e.g. (i) Darwin's finches



(ii) Australian Marsupials



(iii) placental mammal

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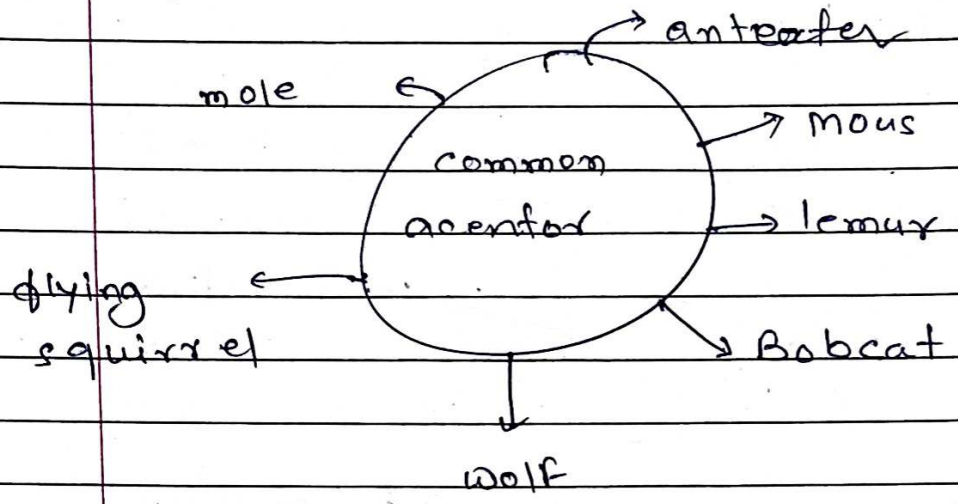
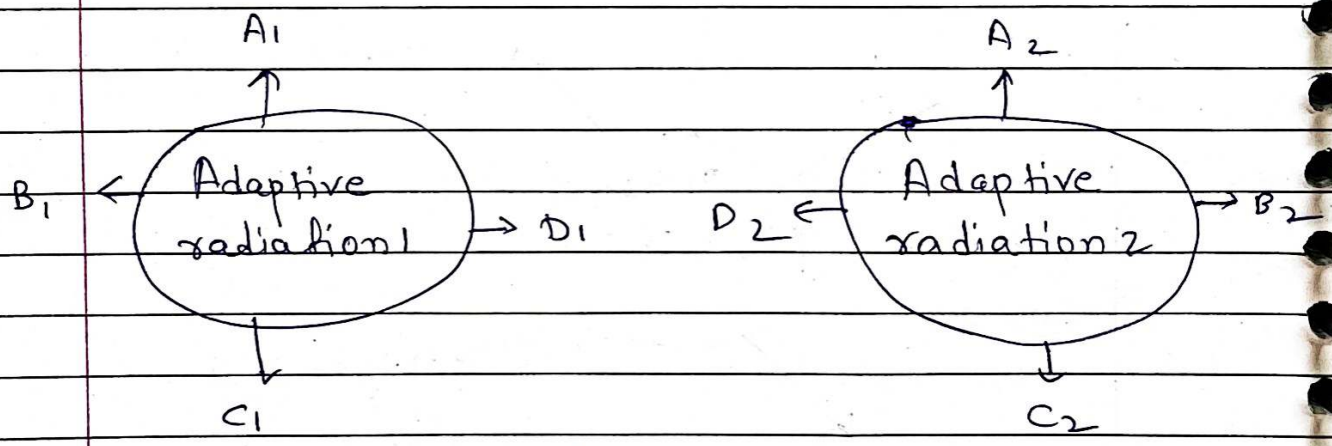


* Convergent evolution

→ When more than 1 adaptive radiation take place at the same gegraphical location, then the members of both radiation show similarities among themselves. (Due to same environment, same need)



In above example, 2 adaptive radiations are taking place at same location.

$A_1 \simeq A_2$ $\quad D_1 \simeq D_2$

$B_1 \simeq B_2$

$C_1 \simeq C_2$ $\quad \simeq$ ← similar

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VVI

Placental mammal		Marsupial mammal
Mole	→	Marsupial mole
Anteater	→	Nubat
Mouse	→	Marsupial mouse
Lemur	→	Spotted cuscus
Flying squirrel	→	flying phalanges
Bobcat	→	Tasmanian tiger cat
Wolf	→	Tasmanian wolf

* Evidences from Connecting link
  - ↳ Organism that connect two groups of organism
  - ↳ Have characters of both group

- Virus ÷ b/w living and non-living
- * Euglena ÷ b/w plants and animal
- Proterospongia ÷ b/w protozoa and poridera
- * Neopilina ÷ b/w Annelida and Mollusca
- * peripatus ÷ b/w Annelida and Arthropoda
- Balanoglossus ÷ b/w Non-chordata & chordata
- Chimera ÷ b/w Cartilaginous and bony fishes
- Protopterus (lung fish) ÷ b/w pisces and Amphibia
- Seymouria ÷ b/w Amphibia and Reptilia
- * Archaeoptery ÷ b/w Reptilia and Aves
- platypus and Echidna ÷ b/w Reptilia and Mammalia

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- Origin of first cellular life form — 2 BYA
- Origin of invertebrate — 500MYA
- Origin of jawless fish — 350MYA
- Sea weeds and plant — 320MYA
-

→ The first organism that invaded land were plants

→ Lobbedfins fish (fish with stout and strong fins) (coelacanth fish) 350MYA move on land and returned back in water. Thought to be extinct. But in 1938 in south Africa this live (living fossil) fish was caught.

→ Lobefins gave rise to first amphibia (lived on both land and water)

→ Amphibia were second organism but first animal that migrated from water to terrestrial habitait.

→ Amphibia gave rise to reptiles. They lay thick shelled eggs (which protect their egg from heat) (terrestial adaptation) (first terrestrial vertebrate)

→ Some reptiles returned back to water and form fish like reptiles (Ichthyosaurs) (200MYA)
↳ Not found now

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* Archeopteryx
↳ connect reptiles and aves

- Reptiles
  ↳ long tail, teeth, weak sternum, heavy bone, free caudal vertebrae

- Aves
  ↳ feathers present, forelimbs, modified into wings, beak present

* Timeline of evolution

ERA (longest)
↓
period
↓
Epoch (smallest)

- Eras

1. Azoic (oldest)
2. Archaeozoic
3. proterzoic
4. palaeozoic
5. Mesozoic
6. Cenozoic (recent)

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- Palaeozoic era
  ↳ period ÷ Cambrian, Ordovician, silurian Devonion (age of fishes), Carboniferous (age of amphibians), permian

- Mesozoic era (age of reptiles)
  ↳ period ÷ Triassic, Jurassic, Cretaceous

- Cenozoic (age of mammals)
  ↳ period ÷ Tertiary, Quaternary

* Origin and Evolution of man

(1) Dryopithecus
→ Arose about 15mya
→ More like ape
→ Hairy
→ Walked like chimpanzee and gorilla
→ Common acentor of man and ape

(2) Ramapithecus
→ Arose about 15mya
→ more man like
→ Oldest human acentor
→ Cranial capacity 600cc

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(3) Australopithecus

→ Connecting link b/w ape and man
→ Man like primates
→ Arose about 2mya
→ Hunted with stone weapons (entertainment)
→ Vegetarian

(4) Homo habilis

→ First human like (hominid)
→ 650–800cc
→ first tool maker
→ Vegetrain
→ fossils found in African caves.

(5) Homo Erectus

→ Arose about 1.5 mya
→ 900cc
→ Used fire and probaly eat meat
→ Fossils were discovered in java in 1891 (java-man), in china (peking man), in Germany (Heiderberg man)

(6) Neanderthal man

→ fossils first obtained from neander valley in Germany
→ Arose about 100000–40000 years back
→ 1400cc
→ Used hides to protect their domestic animals & themselves.
→ Bury their ~~death~~ dead

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⑦ Cromagnon
→ Earliest form of Homo sapiens
→ 1650 cc
→ Cave paintings and arts e.g. Bhimbetkar rock shelter in raisen MP

⑧ Homo sapiens

→ living modern
→ Arose in Africa and moved across continents
→ Agriculture and human settlements.

Dryopithecus → Ramapithecus → Australopithecus → Homo habilis → Homo erectus → Homo neanderthal → Homo sapiens

Dinosaurs (suddenly disappeared around 65 MYA)

Reason : climate change.
· most of them evolved into bird
· ~~Some~~ Small reptiles exist now

→ Birds originated from reptiles (Archeopteryx)

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- Reptiles (Therapsid) gave rise to mammals. first mammals were like shrews

- Mammals were viviparous and more intelligent, which ensures their continuity on land.

Human Health & Disease

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* Good humor hypothesis
  ↳ fluid

- Given by Hippocrate (early Greek thinker)
- Supported by Indian Ayurveda System

- A/c to this theory :-
  balance fluid in body → healthy
  unbalance fluid in body → disease

- Fluid present in body :- blood, cough (plegmn), yellow bile ↳ by liver and blackbile (by spleen & kidney)

e.g. person with more blackbile belong to hot personality and have fever

- This hypothesis disproved by William Harvey
  He discovered blood circulatory system

- He disproved this hypothesis by following experiment :-
  person with more blackbile in body
  ↓
  Normal body temperature

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* Health

- Health does not mean physical fitness or absence of disease.

- Health means Complete well-being in physical, mental and social aspects. (WHO)

- Health :-
  → increase efficiency, productivity and economic prosperity

  → decrease IMR and MMR, increase longevity

- Health is affected by following factor

(i) Genetic disorder / congenital disease
→ inherited disorder, present from birth
e.g. sickle cell anemia, Down syndrome

(ii) Lifestyle
→ eating habit, yoga, exercise, stress, personal hygiene, water intake, alcohol/drugs and sleep cycle

→ involves habits that you have or lack in your dailylife.

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(iii) Infection
→ infection cause by pathogen during life time
→ also known as acquired disease (acquire - during lifetime)

Q. How to be healthy ?
→ Healthy balanced diet
→ Good intake of water
→ Hygiene source of food & water
→ proper disposal of waste
→ personal hygiene
→ Vaccination
→ Awareness about disease
→ proper sleep cycle
→ Exercise/yoga
→ No alcohol and drug abuse

* Disease
dis ease
(un) (comfort~~able~~)

· When one or more organs or organs system do not function effectively.

Disease
↓ Congenital
↓ Acquired

• Contagious disease
→ spreads through physical contact

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• Congenital disease
→ present from birth

• Acquired disease
→ Acquire during life time

Acquired disease

Communicable or infectious disease	Non-communicable or non-infectious disease
→ Can be tranfered easily from one person to another	→ Can't be transmitted from one person to another

Note :- AIDS → fatal infectious disease
Cancer → fatal non-infectious disease

* Pathogen

• Disease causing organism

• Can be virus, bacteria, fungi, helminthes and protozan

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To cause disease, pathogen must survive & grow/multiply in host body

- e.g. Bacteria affecting stomach
  ↳ must survive in low pH & resist - ~~en~~ enzymatic activities

* Typhoid

→ Bacterial pathogen ÷ Salmonella typhi
→ Affect small intestine
→ Circulate to other organs through blood
→ Enters in body through contaminated food and water
→ Symptoms ÷ Stomachache, constipation, weakness, loss of apetite, headache and sustain high fever (39°c – 40°c)
→ Detected through Widal test

- Classic case ÷ Mary Mallon
→ Nickname ÷ Typhoid Mary
→ Cook by profession
→ Asymptomic carrier of typhoid
→ Spread typhoid for many years through food she prepared.

- In severe case ÷ intestinal perforation & dead

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* Pneumonia

→ Cause by bacteria Streptococcus pneumoniae or Haemophilus influenza

→ Affects lungs (alveoli)

→ Due to infection, alveoli become fluid-filled (efficiency of gaseous exchange ↓)

→ Symptoms ÷ cough, chills, headache & fever

→ Severe case ÷ lips, finger nails turn bluish-grey (due to lack of oxygen)

· Mode of transmission ÷ by air droplet, sharing of objects

* Other bacterial disease

(i) Dysentry

→ pathogen ÷ Shigella sonnie, Shigella flexneri & Shigella dysentriae

→ Affects intestine

(ii) plague (Black death)

→ pathogen ÷ Yersinia pestis

→ Affect blood & lymph

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(iii) Diptheria
→ pathogen ÷ Cornyebacterium diphtheria
→ Affect throat, tonsil, nose
→ diagnosis ÷ Schick test

(iv) Tetanus (lock jaw disease)
→ pathogen ÷ Clostridium tetani
→ Affect muscle of neck and jaw

* Common cold

→ Cause by group of virus ÷ Rhino virus
→ Affects respiratory pathway and nose (not lungs)
• Symptoms ÷ headache, nasal congestion, nasal discharge, weakness, sore throat, cough
→ lasts for 3-7 days
→ mode of transmission ÷ by air droplets, by sharing objects

* Other viral disease

(i) polio
→ polio virus (pathogen) (ss RNA)
→ Affects nerves

(ii) Dengue
→ pathogen ÷ dengue virus (arbo virus)
→ Affects liver

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(iii) Chickangunia
→ pathogen ÷ chickangunia virus (toga virus)
→ Affects joints

* Ring worm

→ Caused by fungi genera ÷ microsporum, trichophyton, epidermophyton

→ Symptoms ÷ dry, scaly leison (with intense itching)

→ Heat and humidity provide good environment for growth of fungi

→ Transmit through soil and by using towels, clothes, comb of infected person.

→ Commonly known as Athelete's foot

* Malaria

→ Caused by protozoa plasmodium

· Four species of plasmodium that cause malaria ÷ plasmodium vivax, plasmodium malariae, plasmodium falciparum (fatal) and plasmodium ovale (rare)

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→ Vector of plasmodium ÷ female anopheles mosquito

→ plasmodium needs 2 host (digenetic) to complete its lifecycle ÷ Human & ♀ anopheles mosquito

→ Symptoms ÷ chills and high fever (every 3-4 days)

- Life cycle of plasmodium

infected ♀ anopheles mosquito bite a healthy person

↓

Sporozoite enters in body of person and affect live cell

↓

Sporozoite mutiple asexually in hepatocytes and burst them

↓

Sporozoite enters in RBC of infected person

↓

In RBC ÷
- sporozoite multiply asexually
- Convert haemoglobin into haemzoin
- form gametocyte
- Rupture RBC and release gametocyte and haemzoin

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↓

female anopheles mosquito bite infected person and take blood (includes gametocyte)

↓

Gametocyte enters into gut of mosquito & fertilise

↓

fertilisation and development take place

↓

Sporozoite form, escape to salivary gland and get store there.

↓

When this infected ♀ anopheles mosquito bite ~~unef~~ unaffected man, sporozoite enters in body and cycle continues.

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infected ♀ anopheles mosquito bite healtly person

sporozoite enters in body, sporozoite enters in liver cell, multiple & burst liver cell

Human host

sporozoite enters RBC
- mutiple asexually
- Haemoglobin → haemozoin
- form gametocyte
- rupture RBC

- rupture RBC release haemozoin & gametocyte

♀ anopheles mosquito bite infected person

gametocyte enter in gut of ♀ anopheles mosquito

Fertilisation & development of sporozoite

Mosquito host

Sporozoite Store in salivary gland

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* Amoebiasis (Amoebic dysentry)

→ Due to protozoa Entamoeba histolytica
→ Affect large intestine
→ Spread through contaminated food and water
→ Mechanical carrier = ~~bes~~ house fly
→ Symptoms :- Abodominal pain, cramps, constipation, stool with excess mucous & blood cloat

* Extra points related to Plasmodium

→ In liver cell, sporozoite form Merozoite
→ Merozoite infects RBC
→ Trophozoite stage is formed in RBC which feeds on Haemoglobin

Haemoglobin ⟶ Haemozoin

→ In human

- Exo-erythrocytic cycle → In liver
- Erythrocytic cycle → In RBC

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→ Sexual stage initiated in human and complete in gut of mosquito (♀ anopheles)

· After fertilization of gametocytes in gut of mosquito :-

zygote → ookinete → oocyst (burst) → release sporozoite

→ Sporozoite store in salivary gland

* Helminthic disease

→ Disease cause by worms

(i) Ascariasis

→ Caused by Ascarias (common round worm)
→ Affect intestine
→ Transmitted through contaminated food and water (with eggs of parasite)
· Symptoms :- Muscular pain, internal bleeding Anemia, Intestinal blockage and fever.

(ii) Filariasis / Elephantiasis

→ Caused by filarial worm :- Wuchereria bancrofti & Wuchereria malayi
→ Affect lymphatic vessels of lower limb (mostly)
→ Slowly develop chronic inflammation in the residing organ

→ Also affect structure of genital organ (gross deformities)

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Male ÷ Scrotum
female ÷ breast

→ Transmitted by bitting of ♀ culex mosquito

* Preventive Measures against infections disease

(i) Personal hygiene
→ clean your body properly
→ eat and drink clean water & food

(ii) Public hygiene
→ proper disposal of waste and excreta
→ Clean pools, tanks etc

(iii) For air-borne disease
→ use mask
→ maintain distance from infected person
→ Avoid sharing of object

(iv) for mosquito (insect) borne disease
→ use mosquito net
→ use mesh wire in window and door
→ Avoid stagnation of water
→ insecticide
→ introduce gambusia fish in pond.

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(mosquito) Vector	disease
Anopheles →	Malaria
Culex →	filariasis
Aedes →	dengue and chickungunya

* Immunity

- Ability of host to fight with the disease causing organism (pathogen), is known as Immunity
- Immunity is given by Immune system

Immunity
- ① Innate or congenital immunity
- ② Acquired immunity

① Innate immunity
→ present from birth
→ It is non-specific because it treat all pathogen similary
→ Has no memory
→ prevent entry & growth of pathogen

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② Acquired or Adaptive immunity

→ gain during the life time
→ Highly 'specific' (treat every pathogen ~~specially~~ specifically)
→ Can differentiate b/w self and non-self cell (Discrimination)
→ Has memory

* Innate immunity
↳ It is study under 4 barriers ÷

(i) physical or anatomical barrier
→ prevent entry ~~in~~ of pathogen in body
→ Includes skin and mucus coating/lining.

(ii) physiological barrier
→ provide environment which kill bacteria
→ Include secretions like HCl in stomach (Acid: Anti-bacterial), Tear, caliva etc

(iii) Cellular barrier
→ Include phagocytic cells like ÷
- neutrophils [PMNL] ÷ polymorpho nuclear lymphocyte
- Natural Killer cells
- Monocyte
- Macrophage

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Note: (a) Neutrophil, monocyte and macrophage all phagocytic cell.

(b) Neutrophil, monocyte and monocyte found in blood. Macrophage is found in tissue.

(iv) Cytokine
→ Virally infected cell secretes substance called Interferous (proteinecious) that protects non-infected cell from viral infection

Note: physical + physiological → 1st line of defense
Cellular + cytokine → 2nd line of defense

* Acquired Immunity

- 1° immune response: When the body encounters the pathogen for the 1st time, the response is slower & takes time, but memory is developed (low intensity)

- 2° immune response: When the same pathogen enters in our body next time, due to the memory of previous encounter, this time the response is much faster (High intensity)

- 2° immune response = Anemnestic response

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Acquired immunity

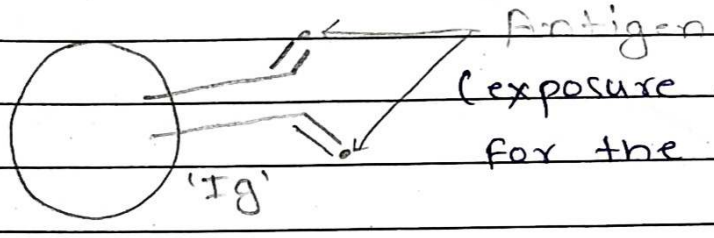
- Humoral immunity
- cell- mediated immunity

- Humoral immunity
→ B-cell / B-lymphocyte involved
→ Secretes antibody / immunoglobulins in blood
→ B-cell
  - → plasma B-cell
  - → Memory B-cell

- Cell- mediated immunity
→ T-cell / T-lymphocytes involved
→ T- cells
  - → T_H (Helper T cell)
  - → T_C (cytotoxic T-cell / killer T-cell)
  - → T_S (suppressor T-cell)
  - → Memory T-cell

* Humoral immunity

- Antigen ÷ Antibody generating substance
(i) Whole organism (pathogen) can be antigenic
(ii) protein express on its surface could be antigenic
(iii) Toxins secreted by them could be antigenic.



(exposure of antigen 'Ag' for the first time)

B-cell

B-cell differentiate into

(i) plasma B-cell
or, Effector B-cell
→ Secrete antibody ('Ig')
during 1° immune
response

(ii) Memory B-cell
→ store for future,
for 2° immune response

- Immunoglobulins (Ig)/ Antibody (Ab)

→ proteinaceous (Glycoprotein) structure
→ 'Ab' represent as :- H_2L_2

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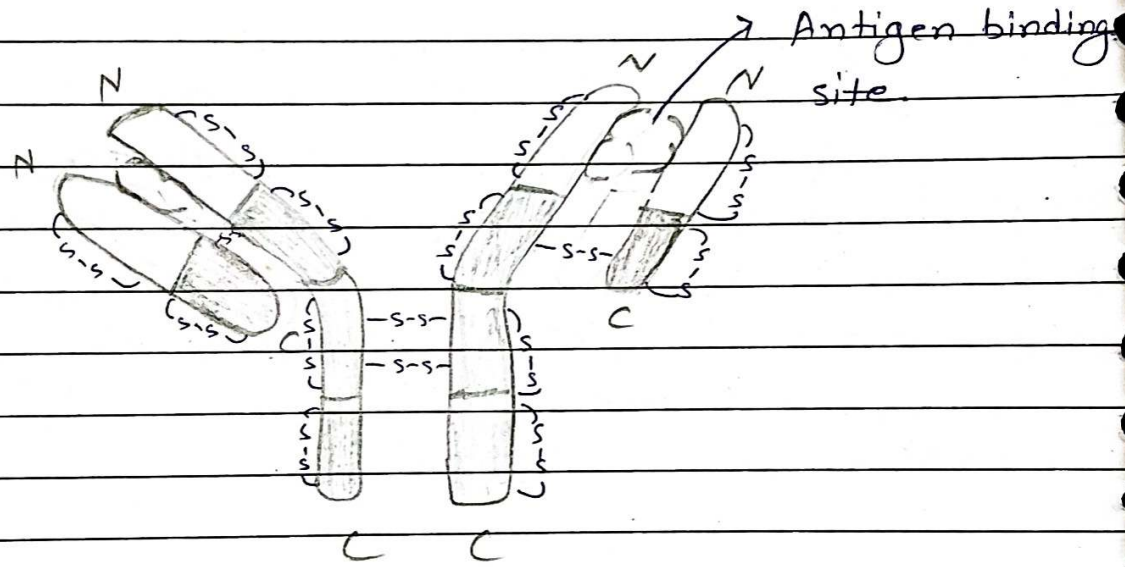
H_2L_2

2 heavy chain
→ Mol. weight 50KDal/each

2 light chain
→ Mol. weight 25 KDal /each

- Structure of antibody



- parotope/antigen binding site
→ Toward N-terminal
→ formed by both heavy & light chain
→ Chains are held together by disulphide
→ Total no. of disulphide bond = 16

- White region is variable region

V_L V_H

↳ variable region of light chain

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- Black region is constant region

C_L C_H

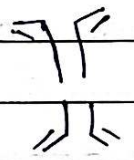
↳ const region of light chain

Note:- Epitope :- Antibody binding site on antigen

* Types of Ig/antibody

(1) IgA

→ 10-15%, Dimer, 4 paratope



→ present in secretion like colostrum, mucus, saliva etc

(2) IgM

→ 7-10%, pentamer, 10 paratope, heaviest antibody

(3) IgG

→ In max^m amount (75-80%), monomer, two paratope

→ Only IgG that cross placenta barrier to provide immunity to foetus.

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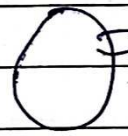
(4) IgE
→ In least amount, monomer, 2 paratope
→ ↑ in allergic response

(5) IgD
→ less than 1%, monomer, two paratope

* Cell-mediated immunity
→ Mediated by T-cells

(i) T_H
→ Secretes substance which help in B-cell differentiation and also help the Tc cell to kill pathogen
→ Also known as CD-4 cell



Tc-cell

(ii) Tc
→ Killer T-cell can directly kill the pathogen
→ Also known as CD-8 cell

(iii) ~~Memom~~ Memory T cell
→ store for future response

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(iv) Ts

→ Suppresses TH & Tc cell for regulated activity time to time and prevent attack on self-cell

* Graft Rejection
  ↳ organ

- for organ transplantation blood group & tissue matching is neccessory

- Cells of our body has certain 'glycoproteins' on its surface called MHC (major histo-compatibility complex)

- Tissue matching = MHC matching

- person with marm matching is selected as donor

- If 'MHC' mismatching is there the cell mediated immunity is responsible for Graft rejection.

Note:- Immunosuppressents like Cyclosporin (obtain from a fugus), Cortisol are often given during transplantation & also life long to prevent unwanted immune ~~respones~~ responses.

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* Active / passive immunity

- Active immunity

→ Body actively form antibodies upon intraction with antigen

→ Takes time but long lasting

→ Memory cells are formed

Active immunity

(i) Natural active immunity

(ii) Artificial active immunity

(i) Natural active immunity

→ In case of any common diseases, pathogens enters and our immune system response and generates memory cells.

(ii) Artificial active immunity

→ Vaccination is case where weak pathogen are introduced into body so that they don't cause disease but activate the immune system to generate memory cells.

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- Passive immunity
→ Antibodies are directly recieved
→ fast action but not long lasting
→ No memory cells formed

Passive immunity

(i) Natural passive immunity

(ii) Artificial passive immunity

(i) Natural passive immunity
→ Ig like 'IgA' in colostrum, IgG via placenta are recieved from mother to the bady naturally

(ii) Arficial passive immunity
→ preformed/readymade antibodies are given for a quick response in case of ÷ snake bite (Antivenom), After cut/injury (ATS)

* Vaccination & Immunisation

→ Vaccination results in Immunisation (development of Immunity)

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- Vaccination is a process in which whole organism (killed & weaked) or surface protein or toxins released or DNA is introduced in body

- purpose of vaccination is to generate memory cells

- Generation of vaccine

- 1st generation vaccine
  ↳ whole organism used (Heat killed or weaked) as vacine

- 2nd generation vaccine
  ↳ A part of organism or toxins used as vaccine

- 3rd generation vaccine
  ↳ DNA of organism used as vaccine

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* Allergy

- Exaggarated (over) immune response of body towards allergens.

- Allergens ÷ pollen grain, dust, mites, a few food items & animal dander (hair) etc

- Upon exposure to allergens redness, swelling (inflammation), sneezing, watery eye, bronchioconstriction & blood pressure reduce (due to histamine) etc occur due to mast cell & basophils (WBC)

- Mast cells & basophils secrete ÷ Histamine, Heparin, serotonin

- Allergy involves IgE, it bind with mast cell & basophils

- prevention ÷ avoid exposure with allergen (wear mask)

- Drugs like Anti-histamine, Adrenaline, Steroids are given to reduce symptoms of allergies

- Ex ÷ Hay fever (against pollen grain), Bronchial asthma

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* Autoimmunity

"Immunity against self is known as Auto-immunity"

. A condition in ~~im~~ which immune system lost the ability to differentiate b/w self & non-self. Hence, start preparing antibodies against self antigen or self-tissue. This condition is known as Autoimmunity resulting in ~~ab~~ Auto immunity disorders.

e.g. Rheumatoid Arthrits, Myasthania Gravis, Hashimoto disease, Vitiligo

* Lymphoid organs -

→ Organ where origin, maturation and proliferation of lymphocytes occur

lymphoid organ

primary | Secondary

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- Primary lymphoid organ

→ Origin and maturation of lymphocytes occur

→ includes :-

① Bone marrow
↳ origin of both B and T lymphocytes
↳ Maturation of B-lymphocyte

② Thymus
↳ lobed organ present near heart, beneath sterum
↳ maturation of T-lymphocyte occur
↳ With age, size of thymus decreases

~~Extra :- MA~~

- Secondary lymphoid organ

→ provide site ~~of~~ for interaction of lymphocytes with antigen.

→ include :- lymphoid node, tonsils, peyer's patches, spleen, Appendix, MALT (mucosa associated lymphoid ~~orga~~ Tissue)

Extra :- MALT constitute 50% of lymphoid tissue in human
Maturation → antigen sensitive

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* AIDS
  ↳ Acquired immuno deficiency Syndrome (group of symptoms)
  - Acquired → gained during lifetime
  - immuno deficiency → immune system ~~weak~~ weak

- First reported case in 1981 (U.S)
- World AIDS day : 1 December

→ In last 25 years, more than 25 million people die because of AIDS.

→ Causative agent ÷ HIV (Human immunodeficiency virus)

- Structure of HIV
  ↳ Retro virus (RNA as genetic material)

→ HIV is enveloped virus.

→ Two ss RNA, Reverse transcriptase (2), also has enzyme Intergase.

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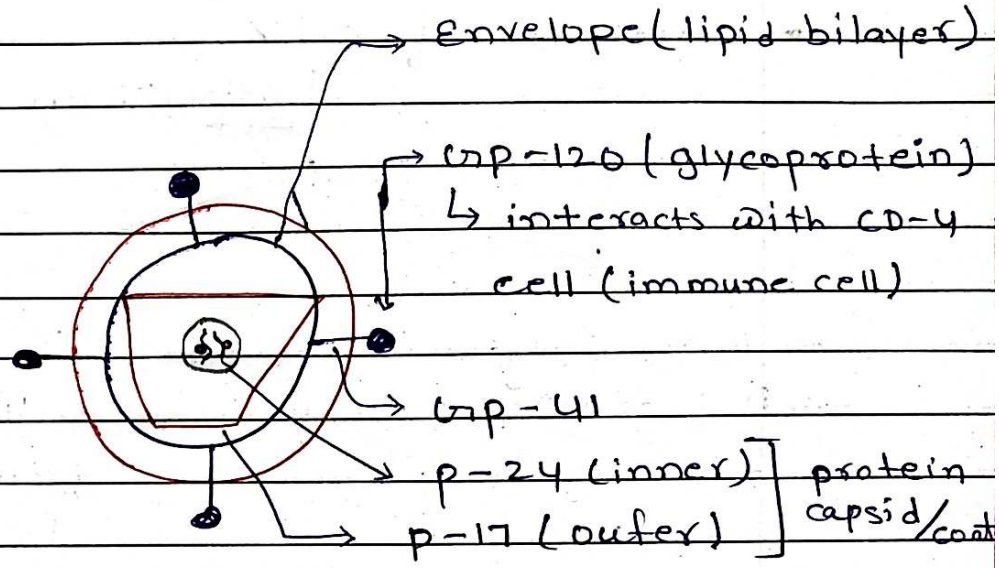

- Mode of ~~Transmition~~ Transmission

→ ~~Infect~~ from infected mother to the foetus
→ By sharing infected nedles (like in case drug abuse)
→ Infected blood transfusion
→ Unprotected sexual intercourse with infected person

- High risk for AIDS

→ Those with multiple sexual partner
→ Drugs abusers (intra vinous injection)
→ Those who require multiple transfusion
→ Children ~~borm~~ born to HIV infected mother

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- Lifecycle of HIV

attacks on ~~act~~

Macrophages
→ Act as HIV-factory

TH cell
→ Their no. reduces from 1200/mm3 of blood to 200/mm3 blood

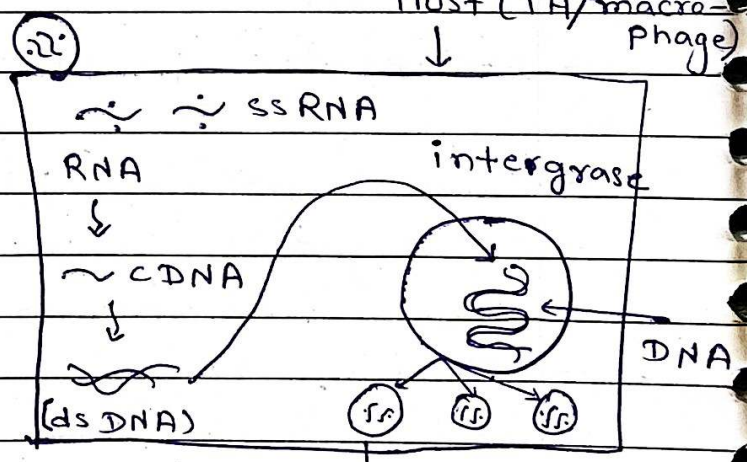
→ Central Dogma

DNA ↻ replication
↓ Transcription
RNA
↓ Translation
protein

RNA
reverse Transcri
cDNA
↳ complement-ary

- integrase enzyme attached virus DNA to host DNA

- Now the virus DNA is a part of host DNA, it uses our machinary to make viral RNA & neccessary protein



↳ New viral progency
ready to attack new cells

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Note: Oppurtunistics infection like by many viruses, fungi, bacteria like mycobaterium (Tuberculosis) Toxoplasma (protozoa causing Toxoplasmosis) may be seen when person suffers from AIDS.

Symptoms: Fever, weightloss, diarrohe is seen & 5-10yr is the time period for the symptoms to appear from time of infection

Diagnosis: ELISA: Enzyme Linked immuno Sorbant Assay (most commonly used diagonstic test)

- Confirmatory Test: Western biotting

- ~~Prev~~ prevention & control

→ Can only be prevented. No cure

- Treatment

↳ Drugs like AZT: Azidothymidine (anti-retero-viral drugs)

↳ It can only ↑ life of patient for few years but can't be cure

- NACO (National AIDS control organization) & other NGOs are working to create awarness & prevention of AIDS

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- WHO is creating safe blood banks, promoting use of disposable needles, free condom distribution, promoting regular health checks.

* Cancer (non-infectious)

→ One of the most dreaded (deadliest) diseasing causing many deaths.

- properties of cancerous cell

① Uncontrolled and Unregulated cell division of cancerous cell ~~is called Tumor~~ form Tumor

② No contact inhibition
(contact inhibition is a property of normal cell which divides & comes in contact with neighbouring cells & stop division which is absent in cancerous cell)

③ Tumor cell take nutrition from normal cell (normal cell become nutrition deprived)

④ Doesn't show Apoptosis (natural cell death)
↳ Cancerous cell became immortal

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- There are some 'regulatory genes' present in our cell, whose breakdown causes cancer

Regulatory gene

① proto oncogenes / cellular oncogenes / c-oncogene

② Tumor suppressor gene

→ Normal gene in our cell, controling cell growth but once activated (mutated) convert into cancer causing ONCOGENES (cancer)

② Tumor suppressor gene

→ Acts as check points for a cell goining through cell division, if division is normal it ~~is not~~ complete division, if abnormal, it is not allowed to go further due to check point

→ If these genes mutated

↓

Cancer might happen

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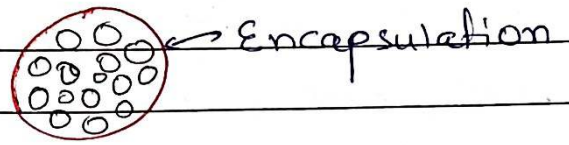
- Types of Tumor

① Benign Tumor

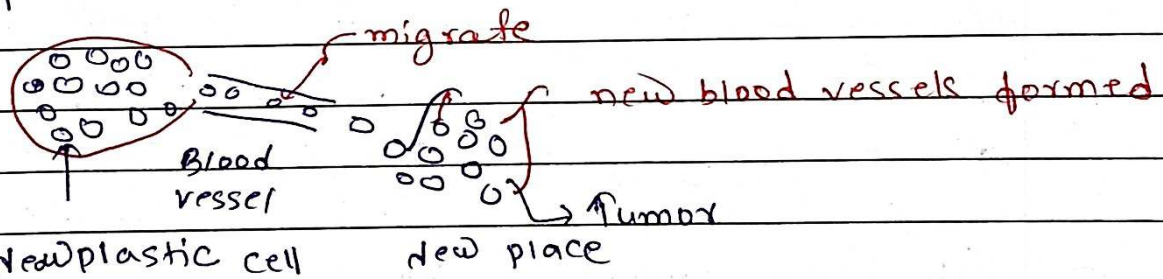
→ It is mass of cell present or localised at a place
→ It is encapsulated (covering around it)



→ No metastasis
→ Non-cancerous, less dangerous

② Malignant Tumor (cancerous, dangerous)

- It is the mass of cells that can potentially breakout of encapsulating & move to new places.



Maligant tume (Neoplasm)

→ Metastasis seen
↳ The property of tumor cell ~~in~~ by which it can move from one place to another

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- Causes of Cancer (Carcinogens are cancer causing agents)

① physical agents
→ radiations like X rays, gamma rays (ionising radiation), UV-rays (non-ionising)

② Chemical agents

→ Tobacco smoking, chewing, soot, coaltar, mustard gas, Asbestos (pollutants) etc

③ Biological agents

→ Virus like HPV (human papilloma virus), HIV, HBV (Hepatitis-B virus) have viral oncogenes

→ can causes changes & mutation in our gene

- Diagonosis

① Biopsy & histopathological study
→ Biospy is make fine section of tissue suspected to be cancerous & then studied under microscope, known as Histopathology

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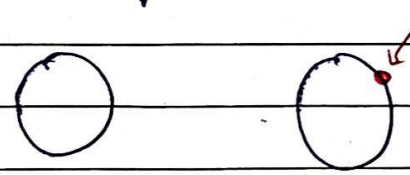
(2) Blood & Bone marrow
→ Usally performed in case of blood cancer (Leukemia), no. of WBC ↑↑

(3) Radiography :- X rays used to obtain 2-D image of internal organ

(4) CT. scan (computed-Tomography)
→ X-rays used to obtain 3D image of internal organ

(5) MRI (Magnetic Resonance imaging)
→ Strong magnetic field used to obtain 3D image of internal organ (safest Technique)

(6) Antibody Test



Note :- If cancer runs in family history, one can pre-diagnose for over-expression of gene.

e.g. Normally : 10000 genes activate

pre-diagnosis : 20000 genes activated

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- Treatment of Cancer

① Surgery
↳ Surgical removal of tumor

② Radiotherapy
↳ Radiation like gamma rays are used specifically to target tumor cells while trying to protect neighbouring cells

③ Chemotherapy
↳ Drugs / medicine / chemicals are used to treat the patients, Side effects like hairloss, Anemia, weightloss seen.

④ Immunotherapy
↳ α - interferons used, these are biological response modifiers, these activate NK cells to target the tumor cell cell

Note :- Combination of these treatment usally given to the patient

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* Drugs

- Drugs are usually the chemical/medicine used for clinical purpose but when misused/abused by people is called Drug abuse.

- Drug abuse is most commonly seen in people of Adolscence age group (12 - 18 yr)

- Addiction: Continous presence of certain chemical constantly required in the body & if a person is stopped from consuming them they show ~~Wit~~ Withdrawl syndrome
  ↓
  group of symptoms like shakiness, sweating, Agressiveness, Nausea

Drugs

1. Tranquillizers
2. Opiods/opiate Narcotics
3. Stimulants
4. Hallucinogens

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① Tranquilizers

e.g. Benzodiazepens, Barbiturates

→ It suppress CNS activity
→ It promotes sleep, bring calmness
→ As clinical significance can be used to treat Insomnia (sleeplessness), As

② Opiods

→ Receptors present on GI tract & CNS
→ They also suppress the CNS activity & slows body function.

e.g. Morphine, Heroin

- Morphine
  ↳ Obtained ~~for~~ from latex of 'poppy plant' (Papaver sominiferum)

→ It is very commonly used as a Sedative & as painkiller (clinical significance) for a patient who has undergone surgery.

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- Heroin
  ↳ It is ~~do~~ diacetylated Morphine
  → Commonly called 'Smack'
  → It is usually snorted or taken intravenously
  → It is white, orderless, crystalline, bitter

Note ÷ Opiods can be Euphoric: (cause Eophoria)
Temporary feeling of happiness

Stimulant

(a) Coca alkaloid (cocaine, crack, coke

→ Coca alkaloid obtained from Erythroxylem coca a native to South america

→ Usually snorted

→ This increase energy, alertness, activity etc

→ It interfers with the transport of the neurotransmitter Dopamine
↓
It level is maintain in the synaptic cleft for a longer time

→ Cause 'Euphoria'
→ Excessive dosage cause Hallucination

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(b) Amphitamines

→ Synthesis in lab
↑ activity, ↑ alertness
→ Sleeplessness
→ Commonly abuse by Sportsperson

(c) Toccabo

→ Consumed by Human more than 400 year
→ Has chemical known as Nicotene
→ Can be taken orally (chewed), snuffed or smoking.

→ Its consumption causes oral cancer, Lung cancer, Urinary bladder cancer, Gastric ulcers, Emphysema, CAD (Coronary artery disease) etc.

· Smoking may also elevate the secretions of Epinephrine & Norepinephrine from Adrenal medulla, this increase Heartrate & Cardiac output. It also increase CO level in body

CO has 200 – 250 time more affinity for Hb than O_2
↓
It binds to Hb
↓
Hence, 'HbO_2' : Oxyhacmoglobin level drop

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* Hallucinogens (Psydelic drugs)

↳ Drugs that cause hallucination
↳ Distorted sense of reality

① Cannabinoids

→ Receptors mainly present in brain
→ Obtained from the inflorescence of plant Canabis sativa

e.g. Mariguana, hashish, charas and ganja
↳ produced by various combinations of flower tops: Leaves, resins

→ Consumed orally or ~~smoked~~ smoked

→ Cause hallucination, affects the Cardio-vascular activity of a person (↑ Heart rate)

→ These days commonly used by sports person

Note ÷ Other hallucinogic plants

Dafura | Atropa belledona

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- Most potent hallucinogen : LSD (Lysergic acid Diethylamide)

Obtained from fungus (Claviceps perpura)

* Anabolic steroids

Synthetic drugs (testosterone derivative), commonly abused by sports person to increase muscle buit, stamina & performance

- Side effect in female

→ Masculinisation (muscle development) (features like males), increased aggressiveness, mood swings, depression, abnormal MC, excessive hair growth on the face and body, enlargement of clitoris, deepening of voice

- Side effects in ♂

→ Acne, increased aggressiveness, mood swings, Depression, reduction of size of testicles, decreased sperm production, potential for - kidney and liver dysfunctic, breast enlargement, premature baldness, enlargement of prostate gland.

Note :- Along with Anabolic steroids, Narcotics (Morphine/Heroin), Diuretics (drugs that promotes Diuresis) also abused

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* Alcohol abuse

- Alcohol is absurbed from GI tract (mainly stomach)
- Cerebellum is affected result in body balancing impaired
- Alcohol: metabolism in Liver

↓

Excess Alcohol consumption

↓

fats starts accumulating in liver

↓

fatty liver

- may also cause severe liver damage :- 'Liver Cirrhosis'
- Alcohol consumption by pregant ♀ cause ~~chan~~ abnormal development in foetus

Note :- Excessive dosage of Drugs/alcohol may cause coma & even death due to heart failure or Cerebral haemorrhage (internal bleeding) or Respiratory failure

- prevention and control

→ Avoid undue peer pressure, Education and counselling, seeking help from parents and peers, looking for danger signs, seeking professional and medical help

Biotech: Principle & processes

* Introduction

- Biotechnology

→ Techiques of using living organism or enzyme from organism for products & services.

- Old/Traditional biotech

→ Techiques of using complete organism like for making curd (lactobacillus), Idli & Dosa (yeast), wine etc.

- Modern biotech

→ Techiques of using GMO (genetically - modified organism) for products & service

e.g. IVF, gene therapy, vaccine, test tube baby etc.

- The European federation of Biotechnology (EFB) has given a definition of biotech that encompasses both traditional view and modern molecular biotechnology. The definition given by EFB is as follows:- The integration of natural science and organism, cells, parts thereof, and molecular analogues for products and services.

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- Molecular analogues
  ↳ oligonucleotide (DNA/RNA), insulin etc made in lab that mimics biological products.

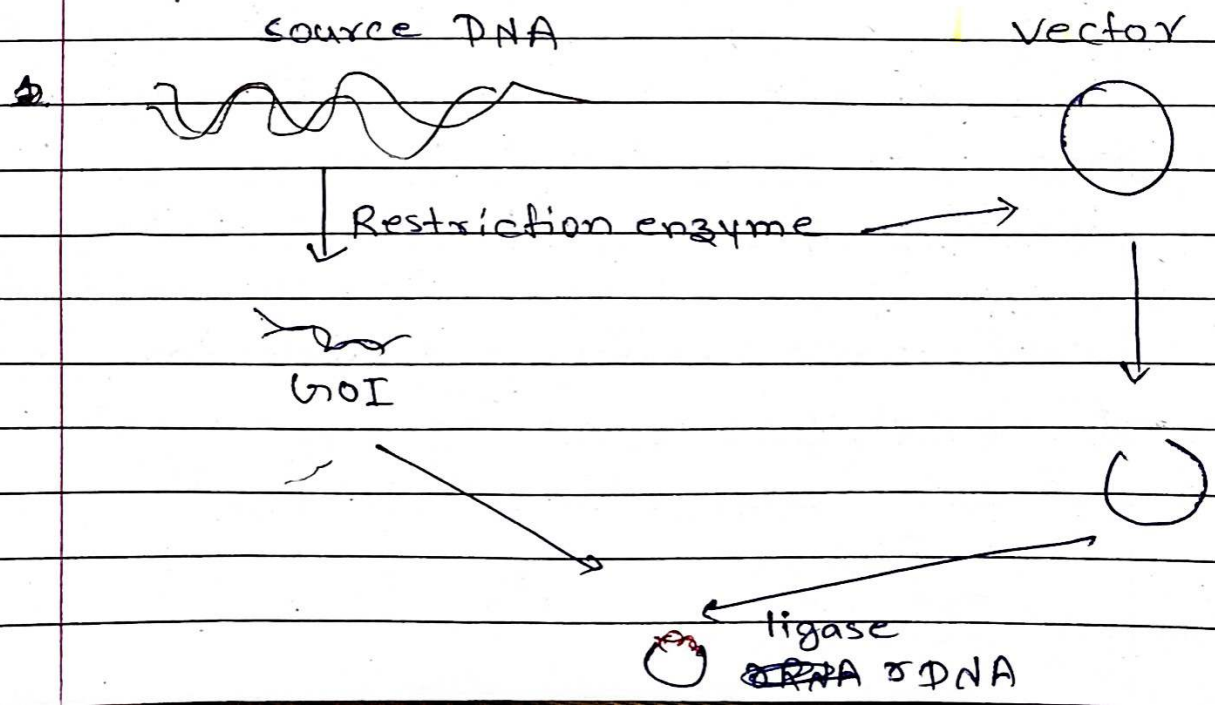
* Principle of Biotech

2 core techniques that enabled the modern biotech.

1. Genetic engineering
2. Bioprocess engineering

* Genetic engineering

- Here we do:
  (i) Construction of rDNA (recombinant DNA)
  (ii) Gene tranfer
  (iii) Gene cloning



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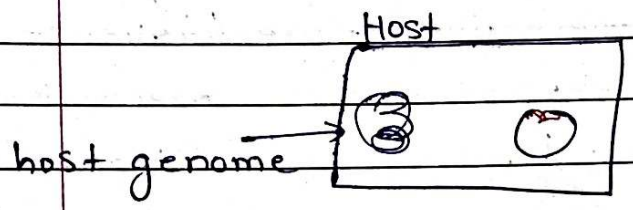
rDNA

$\int$ introduce in host



rDNA multiple, express in host

Tools of recombinant DNA Technology

(1) Lytic enzyme

→ Enzyme that open cell, so that DNA can be extracted for further process.

Cellulose ⟶ for plant cell
lysozyme ⟶ for bacterial cell
pectinase or chitinase ⟶ for fungi

(2) Restriction enzyme

(1) Discovery in 1963, 2 enzyme were discovered in bacteria.

$\int$

When bacteriophage attack bacteria (E. coli)

2 enzymes play role (defense mechanism of bacteria)

1st enzyme add methyl group to own genome

Methylation cause protection of own DNA

2nd enzyme cleave foreign genome

Restriction Endonuclease enzyme

- Restriction enzyme is named so because it restrict the growth of foreign DNA
- 1st restriction enzyme discovered - Hind II (characterization 5 year later)
- More than 900 restriction enzymes have been isolated from 230 strains of bacteria
- Restriction enzyme belong to Nuclease family (break phosphodiester bond)

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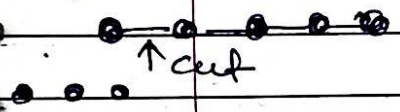
Nuclease

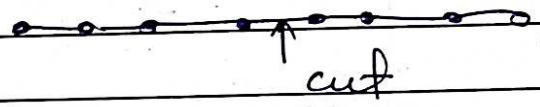
Exonuclease

→ cut at terminal or end
→ chop nucleotide from end



Endonuclease

→ cut in b/w or within



Endonuclease

specific

→ Specific in nature
→ cut at or near recognition sequence
→ It is of 2 types

non-specific

→ non-specific in nature
→ cut anywhere within DNA sequence

Type-I

→ cleave + methylation both property

Type-II

→ only cut property
→ cut at recognition site
→ require Mg^{2+} (no ATP)
→ mostly use in Biotech

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Type-I
→ Cut far from recognition site.
→ require ATP and Mg^{2+}
→ rarely used in biotech

- Naming of Restriction enzyme

EcoRI → order of isolation
↳ strain
genus
Species

Restriction enzyme	Source
(a) BamHI	Bacillus amyloliquefacien H
(b) EcoRI	Escherichia coli RY13
(c) EcoRV	Strain of E. coli "
(d) Sal I	Streptomyces albus
(e) HindII	Haemophilus influenzae Rd

- Restriction enzyme cut at restriction site

- Recognition sequence is the sequence of base pair where Restriction enzyme bind.

- Polindromes :- English words which spell same in forward ~~and~~ as well as reverse direction

e.g. MADAM, MOM

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- Polindromic sequence :- Sequence of DNA which read same when orientation is kept same

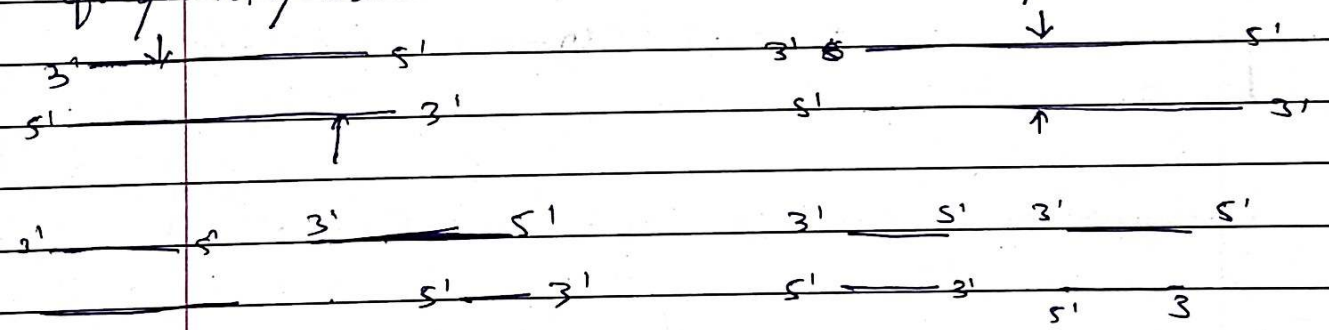
3' — GAATTC — 5' → 5' to 3' (CTTAAG)

5' — CTTAAG — 3' → 3' to 5' (GAATTC)

- Restriction enzyme produce two types of end

Sticky end (cohesive end)
→ Overhanging stretch present
→ Make ligation process easier
→ frequently used

non-cohesive
Blunt end
→ No overhanging stretch
→ rarely used



Note :- Alway we used same restriction enzyme to treat our GOI and Vector. So that same type of sticky end is produced and ligation will be easy.

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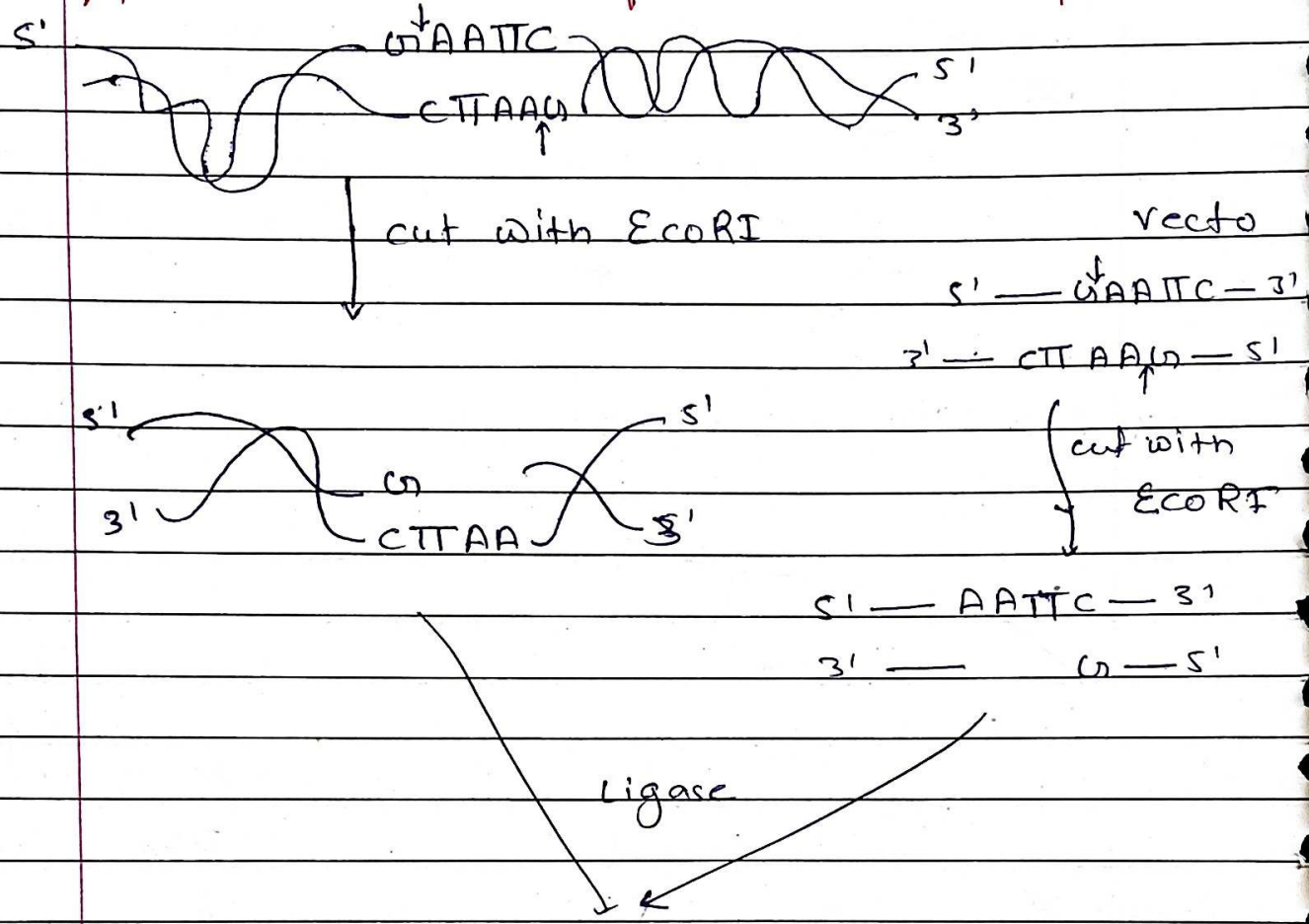
- Action mechanism of Restriction enzyme



- Blunt end produce by :- EcoRV, HinII
- Sticky end produce by :- EcoRI, SalI, ~~Bam~~ BamHI

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(3) Ligase

→ Enzyme that perfor ligation
→ form phosphodiester bond b/w 2 adjacent nucleotides
→ Energy dependent process
→ Known as Genetic glue or gum

(4) ~~Poly~~ polymerase Enzyme

→ polymerase enzyme join nucleotides to form complementary DNA strand

→ DNA polymerase has two 2 activity

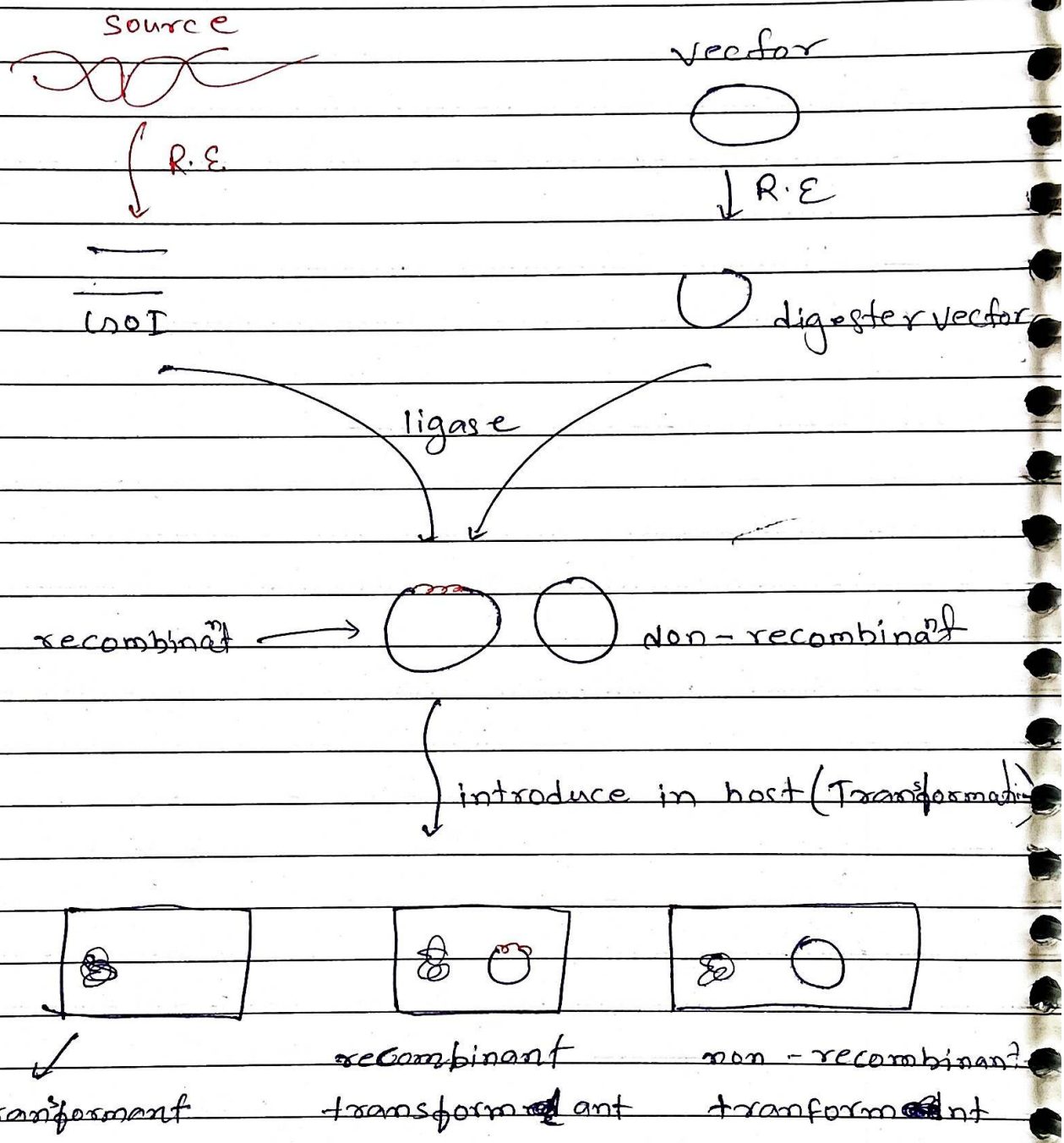
(a) polymerization (5' → 3' direction)

(b) proof-read (~~ch~~ check) (3' → 5' direction)

(5) Cloning Vector

→ Carrier of GOI that can be clone (multiplied)
→ It can be plasmid, Bacteriophage, YAC, BAC

→ We always use cloning vector with high copy numbers.
more copy no. → more multiplication


source
R.E
GOI
vector
R.E
digester vector
ligase
recombinant
non-recombinant
introduce in host (Transformation)
non-transformant
recombinant transformant
non-recombinant transformant

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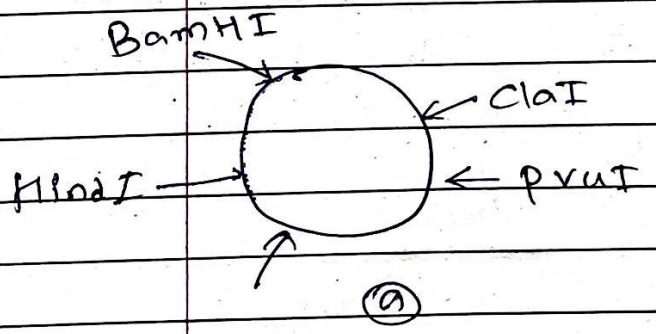
• Characteristics of cloning vector

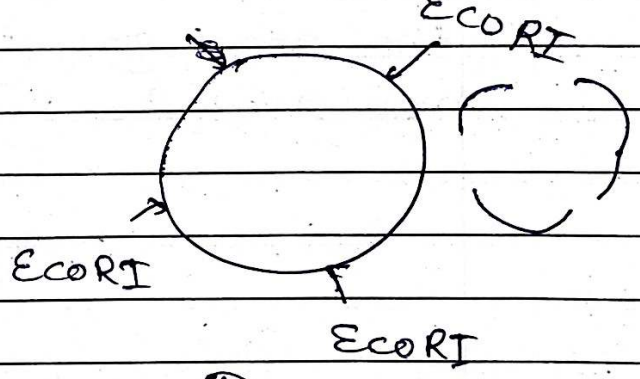
ⓐ Ori
→ Ori stands for origin of replication.
→ Sequence of DNA from where replication start
→ Ori support copy number.

ⓑ Rop
→ Sequence of DNA ~~where~~ which code for protein essential for replication

ⓒ Cloning site
→ Site where restriction enzyme cut
→ Vector with cloning site of different restriction enzyme is selected.
→ Vector with many cloning site of single restriction enzyme is not selected (result in fragments)



ⓐ
Choose



ⓑ
Not choose

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(4) Selectable marker

→ Property of vector which help us in - identifying (selection) transformant and non- tranformant or recombinant and non- recombinant

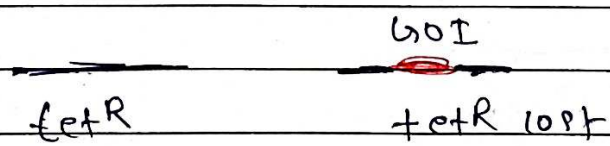
→ Mostly selectable marker are antibiotic resistance gene

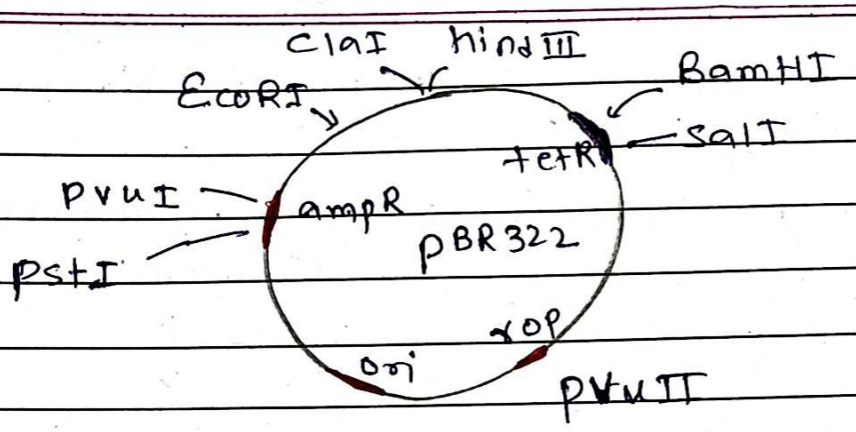
→ Normally E. coli lack resistance against antibiotic

e.g. ampicillin resistance
tetracycline resistance
Chloramphenicol resistance
Kanamycin resistance

- insertional inactivation

→ When we insert our GOI in antibiotic resistance gene (selectable mark), then the gene get inactivated due to insertion and antibiotic property is lost.

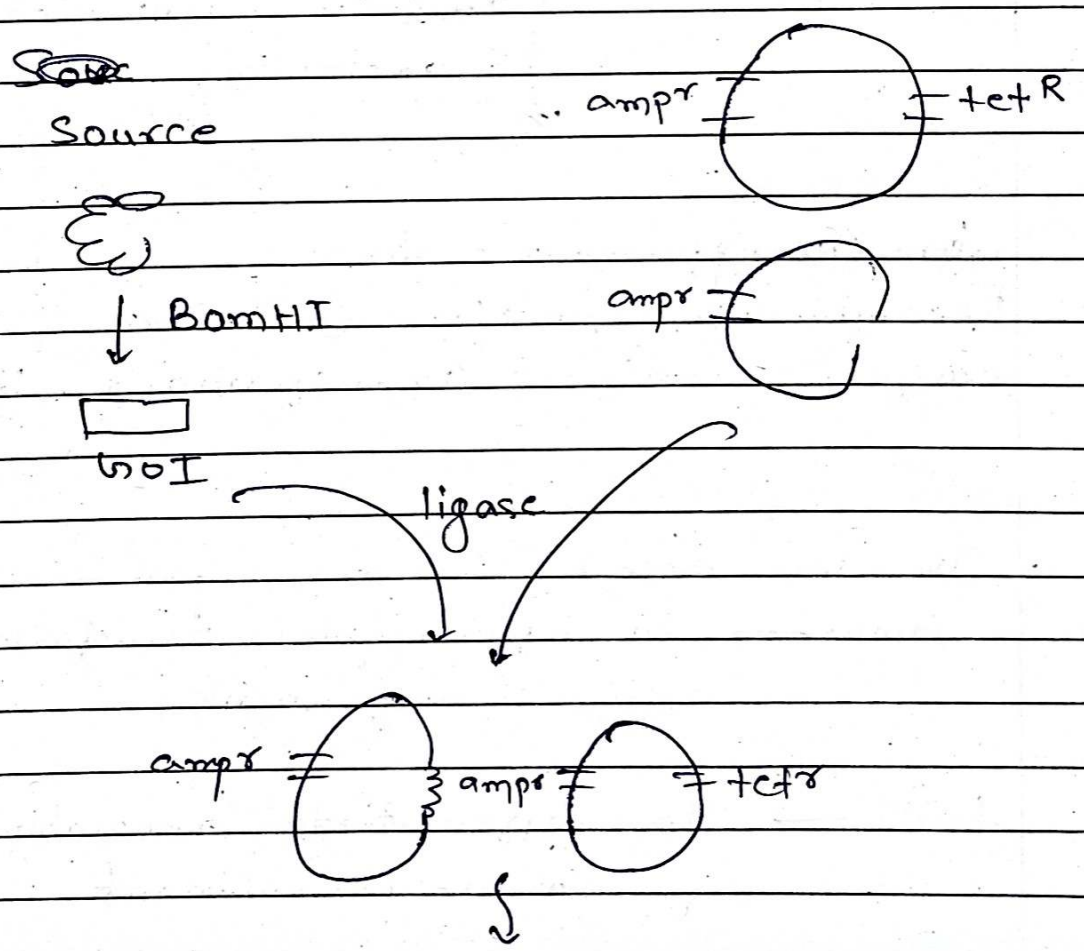




→ 8 cloning site
→ 2 selectable marker

p = plasmid
B = Bolivar
R = Rodriguez
322 = no. of experim

Note :- BamHI, SalI present in tetR
PvuI, PstI present in ampr



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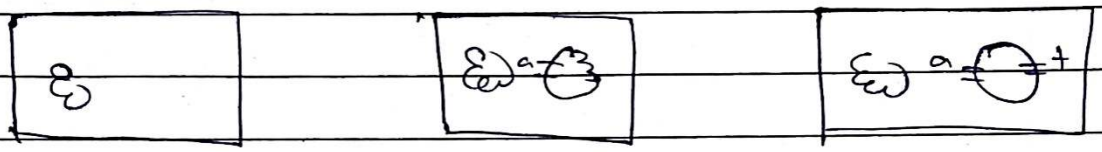
recombinant
non-recombinant } ~~non-recombinant~~

→ grow in medium containing tetracycline

↓

non-recombinant live and recombinant die

Transformation



Non-Transformant | recombinant Transformant | Non-recombinant Transformant

grow in medium containing ampicillin

Non-Transformant = die
Recombinant Transformant = live
Non-recombinant Transformant = live

- In this case,
  Amp^r → to differentiate transformant & non-transformant

  tet^R → to differentiate recombinant & non-recombinant

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	tet^r	amp^r
Recomb – Transformant	✓	✓
Non-recomb – transformant	✓	✓
Non-transformant	✗	✗

- lacZ gene as Selectable Marker

→ Above mentioned process, require 2 plating (tetracycline and ampicillin) which is a tough process.

→ Scientists start using gene as selectable marker that codes for protein which converst substrate into color product.

→ Normally,

lacZ gen

↓ encodes

B - galactosidase enzyme

Xgal (substrate) → blue color product

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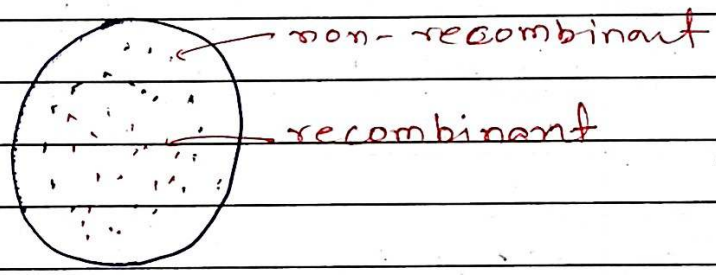
GOI

→ GOI inserted in lacZ gene, lacZ gef inactivated, NO B-galactosidase, NO conversion of X-gal, White color appear

- In this, we get 2 color colony :-
  (i) Blue color → Non-recombinant
  (ii) White color → Recombinant

This is known as Blue-White color screening



- Other cloning vectors

(i) Bacteriophage :- Virus that attacks on bacteria
(ii) plasmid :- (Important pBR322)
(iii) BAC :- Bacterial artificial chromosome. (cc = upto 350 Kb)
(iv) YAC :- Yeast artificial chromosome (cc = 1 mb)
(v) Cosmid (cos site + plasmid) (cc = 30 - 45 Kbp
(vi) phagemid (bacteriophage + plasmid) (cc = upto 10 Kb)

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- Carrying capacity (CC)

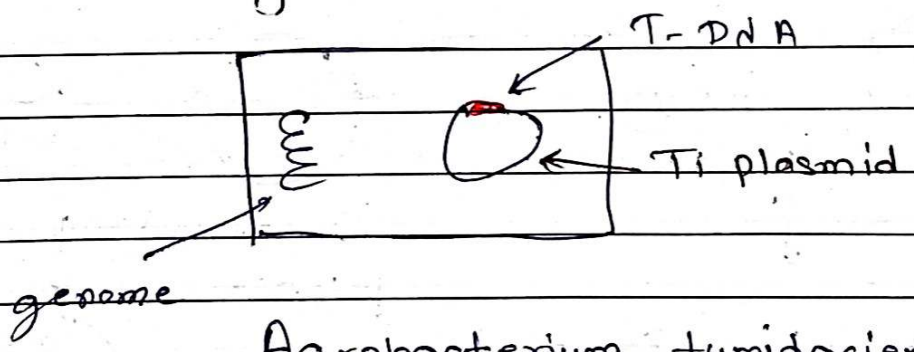
→ Length of GOI that can be carried by vector

- Cloning vector for plant

→ Agrobacterium tumifacien is a pathogen for several dicot plant

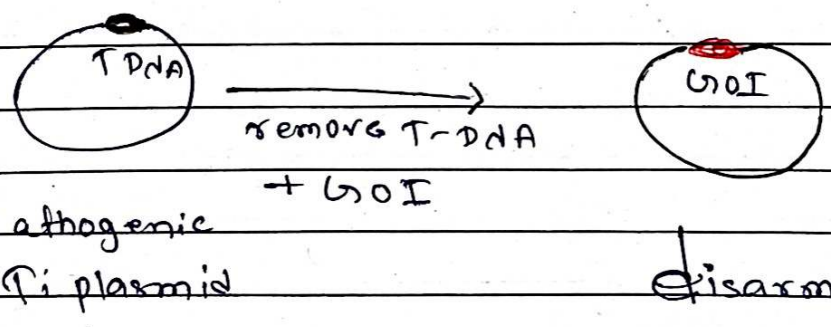
→ It has Ti plasmid (tumor inducing) which has T-DNA (transfer DNA)

→ When T-DNA get incorporated in plant's genome it cause tumor or node, known as Crown gall disease



Agrobacterium tumifacien

- (disarm) modified Ti plasmid is used as vector in plant.



- no T-DNA
- no pathogenicity
- acts as carrier

- Cloning vector for animal

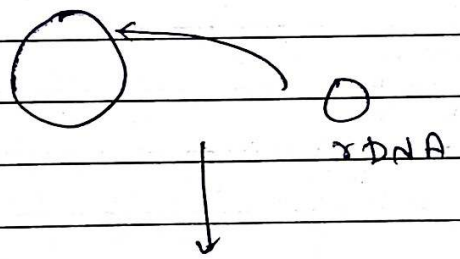
→ Retrovirus are disarm and then used as cloning (- pathogen gene) vector in animal

⑥ Competent host

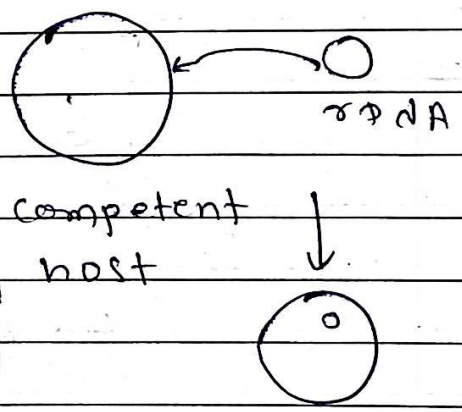
→ Compentent hosts are those hosts that is ready to take foreign DNA

→ Compentent host is ready for transformation

→ To make host competent, we treat them with divalent cation (Ca^{2+})



No tranformation as host is not competent



Competent host accept rDNA

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- Method of transformation

① Heat shock treatment

Competent host + rDNA (incubate)

↓

ice
↓
42°C
↓
ice

Sudden change in tem. cause formation of pores in cell membrane of host enabling entry of rDNA

② Gene-gun or Biolistic
→ for plant
→ micro-particle of tungsten and gold coated with rDNA is bombarded on plant cell with high velocity.

③ Micro-injection
→ Needles carrying rDNA deliver rDNA directly in nucleus of animal cell.

④ Electroporation
→ Use of voltage to create pores in cell-membrane of host to enable entry of rDNA

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(v) Disarmed vector
→ e.g. Ti plasmid for plant
retrovirus for animal

Note:- DNA is hydrophilic
, cell mem. interior hydrophobic (that's why DNA can not enter in cell directly.

Gel Electrophoresis

- purpose
  ↳ Seperate DNA fragments (basis - their size)

→ DNA is -ve charged (due to phosphate), forced to move toward +ve terminal (anode) in an electric field on the basis of their size

→ Smaller fragments move fast (away from cathode) & larger fragments move slow

→ Matrix is made of agarose (natural polymer) (extracted from sea weed)

→ Ethidium bromide (Etbr) is used as stain that is used for visualisation of DNA fragment

→ Under UV ray, visualisation is done

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→ Bright organ color bands are observed under UV-light

→ Desired DNA fragment is cut out of gel, and this process is known as Elution process.

Note:-
- ↳ Ethidium bromide is carcinogenic
- → Combs are used to prepare walls
- → In wells DNA sample is loaded
- → Ladder is used as reference for size of DNA

• Steps in Gel Electrophoresis

(1) prepare gel (with the help of agarose)

(2) Cast gel in tray (use comb to make wells)

(3) Rest the gel for solidification

(4) Remove comb (wells are formed at cathode site)

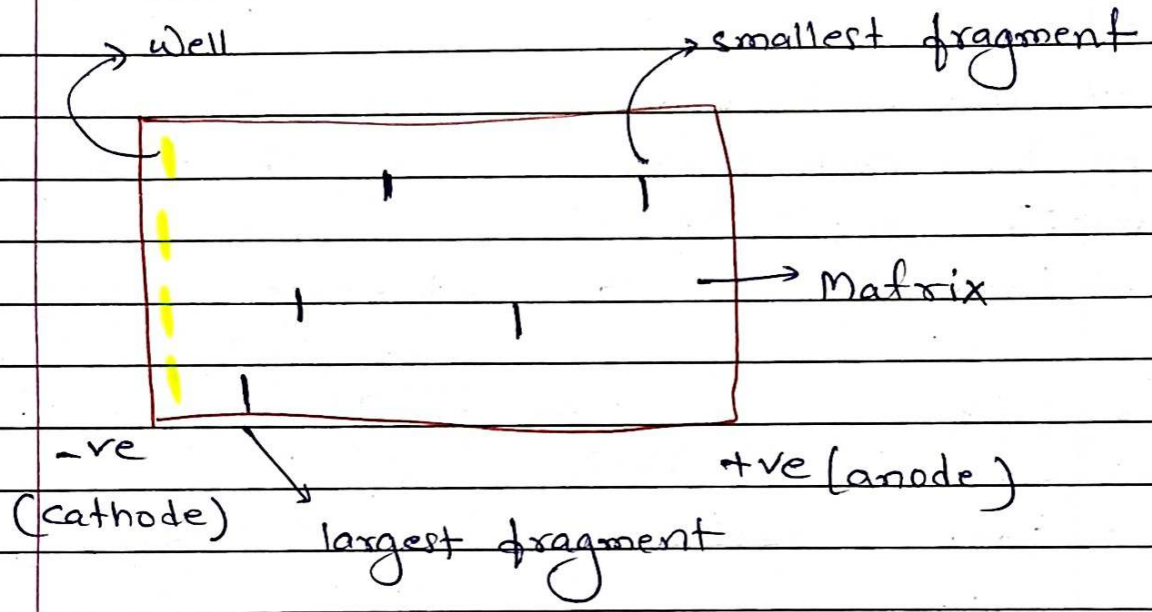
(5) Load DNA is wells

(6) Switch ON the power supply

(7) DNA fragments move towards anode (small = fast, large = slow)

(8) Observe the DNA under UV rays.

Note:- DNA fragments are seprated through — sieving effect.



(Gel Electrophoresis)

* PCR

→ PCR stands for polymerase chain reaction
→ Give by Kary Mullis in 1983
→ ATM:- In vitro replication, make multiple copies of DNA fragment (GDI)

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- Requirements for PCR :-

(i) Tempelate DNA
(ii) DNA polymerase
(iii) Primers
(iv) dNTP
(v) Mg^{2+}, buffer

- 3 steps in PCR
(i) Denaturation
(ii) Annealing
(iii) Extension

(i) Denaturation
→ Ds DNA is seperated at high temperature (95°c)
→ H-bonds b/w nitrogen base pairs are broken (A=T) (G≡C)

(ii) Annealing

→ ~~Forme~~ forward and reverse primers are joined at both strand of DNA

→ Annealing temperature = 40-65°c

→ Primers.
↳ Oligonucleotide sequence provided, which give free 3' OH for extension process

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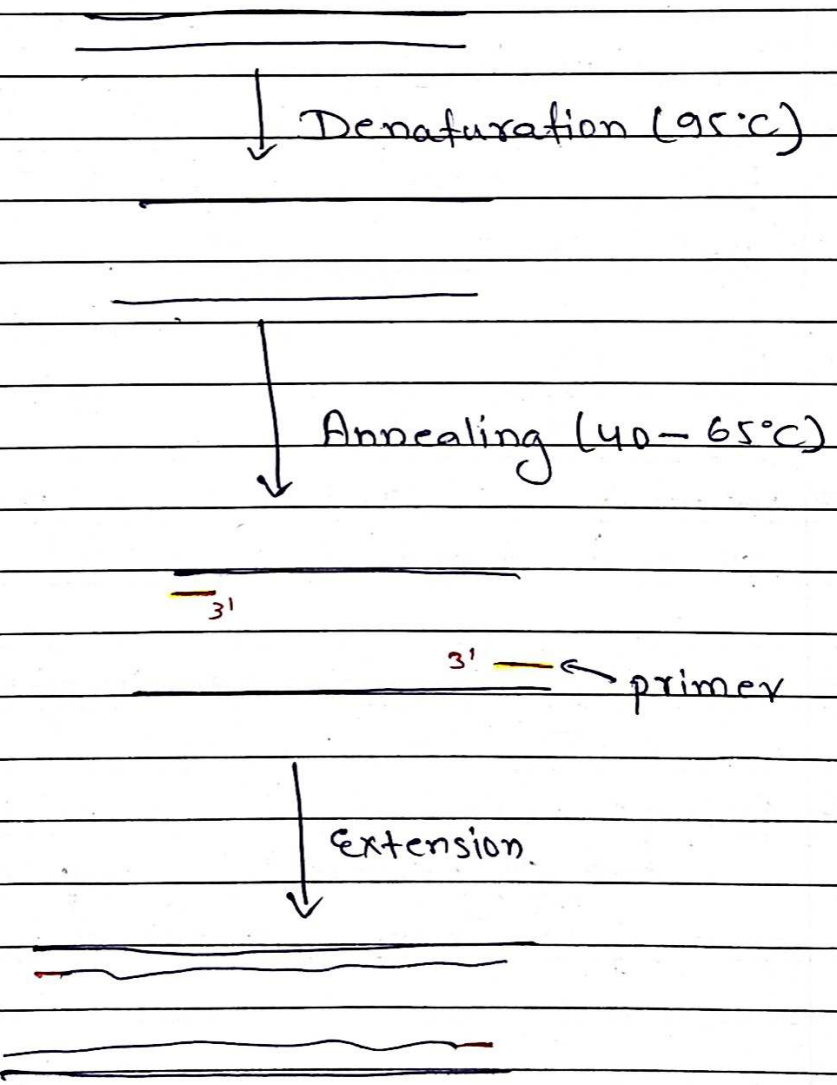
(3) Extension

→ DNA polymerase polymerise the complementary sequence (at 72°C)

→ Taq polymerase is used.

- ↳ thermostable
- ↳ Active at high temperature
- ↳ obtained from Thermus aquaticus



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Note:-

(i) No. of copies of DNA = 2^n (n = no. of cycle)

(ii) After 30 cycles 1 billion copies of DNA obtained

• Application of PCR :-

(i) DNA fingerprinting (ii) forensic science
(iii) Dectection of pathogen (iv) Dectection of mutated gene (v) Prenatal diagonsis ~~etc~~ (vi) gene therapy

* Steps in recombinant biotech

(1) Isolation of DNA

→ DNA is genetic material in most of organism
→ DNA is present inside cell, So to obtain DNA we have to break cell

Component	Treatment
Cell wall →	lysozyme (bacteria), cellulose (plant), pectinase & chitinase (fungi)
Cell mem. →	detergen/lipase
RNA →	Ribonuclease
protein →	protease
Carbohydrate →	Amylase
Lipid →	lipase

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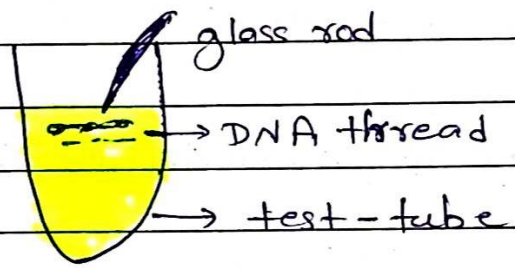
Note :- No use of DNase because we want to isolate DNA

→ We will precipitate DNA with the help of Chilled Ethanol.

→ With the help of glassrod we will take out DNA thread, this process is known as Spooling



Spooling

(2) Cut GOI and Vector

→ Cut at specific location in source DNA and vector DNA with same Restriction enzyme (molecular scissor)

→ DNA fragments seprated on Gel Electrophoresis

→ Both GOI and digested vector is isolated.

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(3) Make multiple copies of GOI (By PCR)

(4) ligation of GOI and Vector with the help of ligase (Genetic glue/gum)

(5) Insert rDNA into host (Transformation)

(6) Select our recombinant transformant with the help of selectable marker

(7) Produce at large scale

(8) Downstream processing

* Bioreacter

→ To produce product at, large scale, bioreacter are used.

→ Bioreactors are large vessel in which 100 – 1000L culture is prepared.

→ Raw materials are provided & optimal conditions are given so that good quality product is produce.

→ Continous stirred bioreacters are most commonly used.

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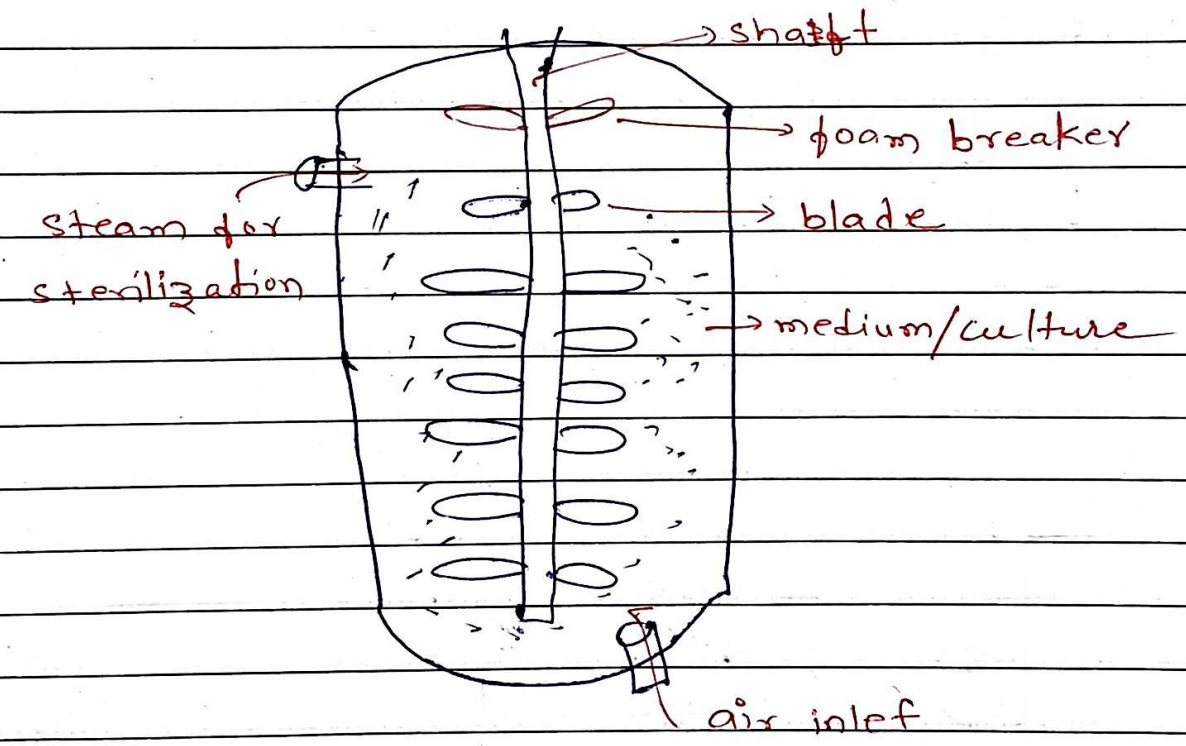
Types of bioreactor

- Simple-stirred bioreacter
- Sparged bioreactor
  - gas is provided in the form of bubbles to increase efficiency



Bioreacter

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Component of bioreacter

(i) Vessel (cylindrical or curved base)
(ii) Sensors for tem. & pH
(iii) Agitator system (motor, shaft, impeller for homogenous mixing)
(iv) Gas/oxygen delivery system
(v) Foam control/braker
(vi) Temperature control
(vii) pH control

* Continous culture system

→ Open type
→ used medium is drained out from one side
→ fresh medium is added from other side
→ most active log phase
→ high yields.

* Batch culture system

→ closed type
→ One time medium addition and output recovered.
→ log phase is short.

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* Downstream processing

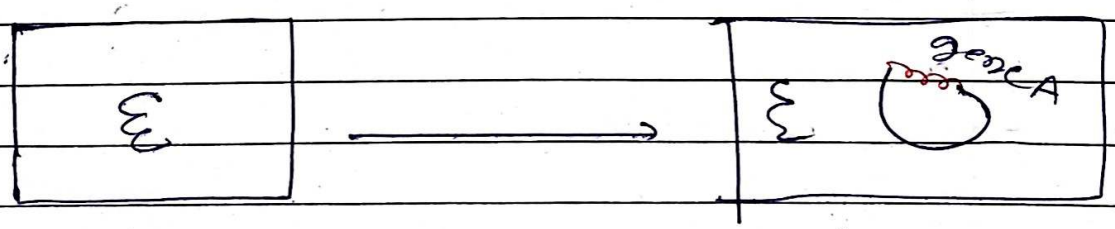
→ Includes steps after production of products
→ like :- seperation, purification, addition of preservative, Clinical trails (drugs), Quality check

ote :- Different product has different downstream process.

* Heterologus protein

→ protein enceding gene expressed in heterologus host.

- Heterologus host
  - → Host in which naturally that protein is absent
  - → When we insert rDNA (having that gene) then host express that protein



bacteria
enzyme 'A' absent

bacteria
enzyme 'A' present
↓
protein A heterologous
Bacteria hetero-logous.

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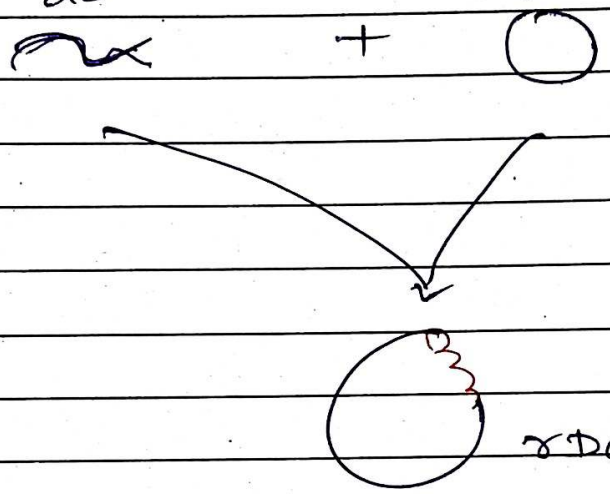
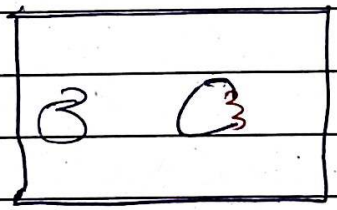
★ Construction of 1st rDNA

→ By Stanely Cohen & Herbert Boyer (1972)

→ ab^r + plasmid (Salmonella typhi)



↓ inserted in E. coli



↳ show ab^r property

Biotech and its Application

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* Introduction

Application of Biotech (majorly)

① Agriculture
↳ Use of 'Genetically modified crop'

② Medicine
→ Biopharmaceutics (drugs/medicine prepared using GMO)
→ Biotherapeutics (use for therapy & treatment of Diseases)
→ Diagnosis (PCR, ELISA)

③ Waste treatment
④ Bioremediation (use of living organism for treatment of H_2O/ soil/ Air pollution)
⑤ Energy production. (Biogas)

* Three critical research area in biotech

① finding the best catalyst in the form of improved organism which is a microbe or pure enzyme

② Creating ~~optium~~ optimum conditions for catalyst to act

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③ Down stream processing

* ~~Biotechno~~ Application of biotech in Agriculture

There are three ways to increase food production

① Use of harmful chemical (Agro-chemical based Agriculture)
e.g. fertilizers, pesticides

② Organic farming: Biofertilizers, Biopesticide
e.g. N_2 fixing bacteria

③ Use of GMC
• Green Revolution

→ Norman E. Borlaug → father of green revolution (globally)

→ M.S. Swaminathan → father of green revolution in India

→ Because of green revolution in India food production increase 3 times but wasn't enough for ~~po~~ increasing ~~popult~~ population.

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→ Food production increase 3 times due to:-

① Better management practices (Bette irrigation, machines, croprotation)

② Used of fertilisers, pesticides

③ Improved Cropvarieties

* Genetically modified Crops:-

① Can tolerate any abiotic stress (Tem/pH/Salinity etc)

② ↑ productivity

③ Reduced reliance (dependency) on pesticides, fertilisers.

④ Make pest-resistant plant (Bt-cotton)

⑤ Better or ↑ mineral usage from soil by plant

⑥ Reduced post-harvest loss
e.g. ~~Flawer~~ flaver savr Tomato
↳ Gene silencing used

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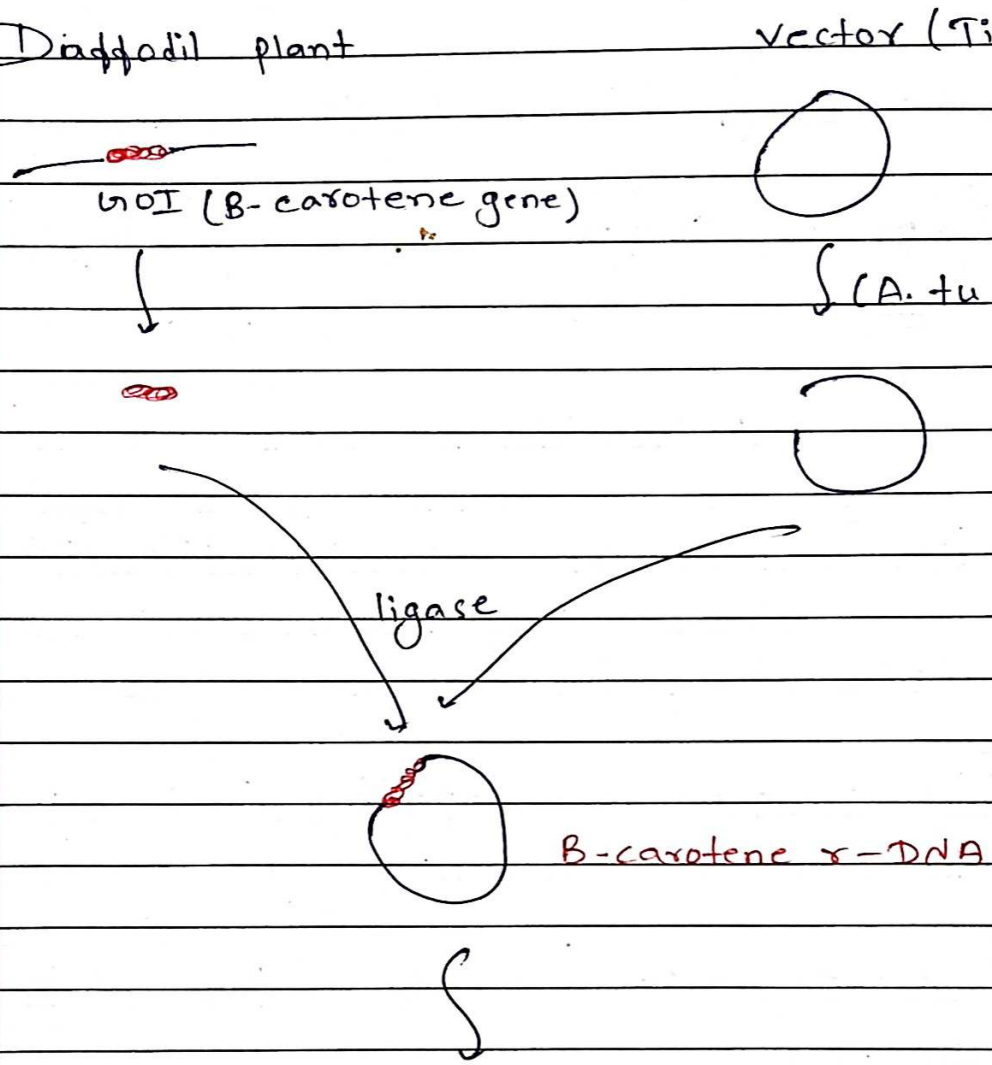
(7) Enhanced Nutritional value

e.g. Golden Rice (vit-A enrichment)



Inserted in Normal rice grain variety (plant)

synthesise/ form

B- Carotene

Eventually form vit-A

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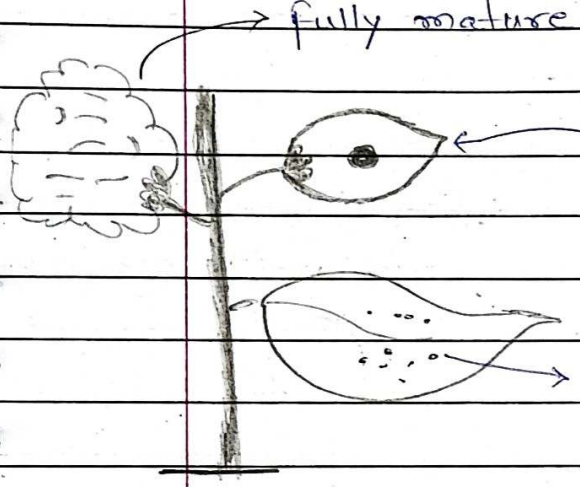
Bt - cotton (pest - resistant plant)



↓

found occasionally on cotton plants

↓

It was observed that if 'cotton'-Bollworms (insect) feeds on this plant & eats the bacteria

↓

It dies

Bacillus thuringiensis

↓

cry gene

↓

At particular phase of growth, cry gene form cry protein

Date ___/___/___
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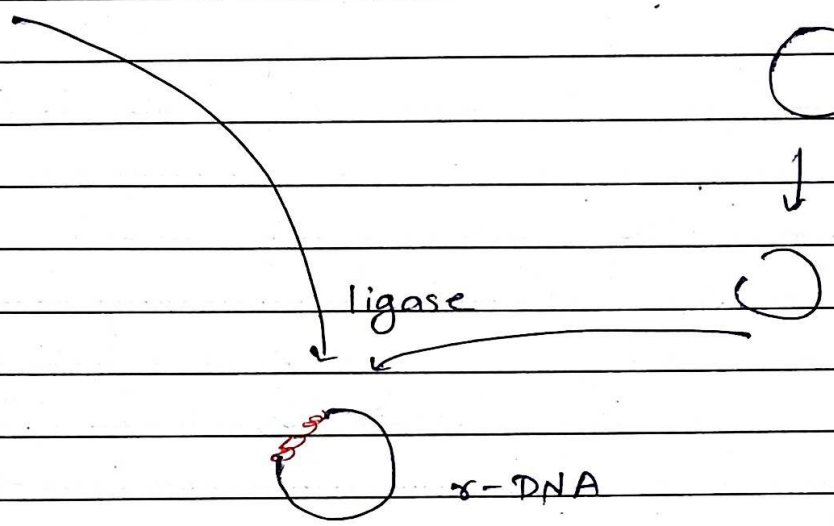
- ~~Car~~ Cry protein
  - → Endo-toxic
  - → protoxin

cry gene

~~Bt - cotton~~
vector (Ti plasmid)



↓

inserted in cotton plants

↓

cry gene

↓

cry protein (inactive)

↓

Insect (cotton ballworm) eats plant

↓

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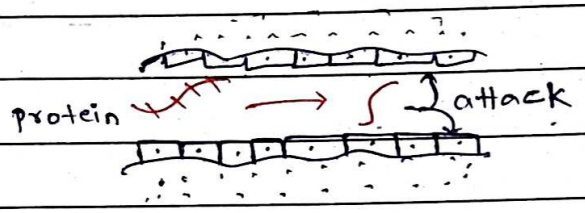
Page_____

Cry protein enters inside insect ~~body~~

↓



epithelial cells of midgut of insect

- In the alkaline pH of midgut these protein get activated

↓

Causes pores in Epithelial cell

↓

Fluid from surrounding enters cell

↓

Cell swells & burst

↓

insect die

Date ___/___/___
Page _____

- Some important points

① Choice of cry gene depends on → The pest & crop

② Cry IAb → Corn borer

③ Cry II Ab, cry I Ac → cotton bollworm

Extra ③ Phylum Arthropoda

↓

Class Insecta

↓

Orders

- → Lepidopterens : Tobacobudworm, Army-worm, Cotton bollworm
- → Coleopterens: Beetles
- → Dipterens: flies, Mosquito

Cry protein is toxic

Date ___/___/___
Page _____

* RNAi / m-RNA silencing
↳ RNA interference

Replication ↻ DNA

↓ Transcription

mRNA

↓ Translation

protein

- In gene silencing : mRNA needs to be silent
  ↳ Done by making dsRNA
  ↓
  No protein

Note:-

(i) RNAi takes place in all eukaryotes as a mechanism of natural cellular defense

(ii) Here, the source of complimentary mRNA is through infection of RNA virus. or Transposons (Jumping gene) that replicate via RNA intermediate.

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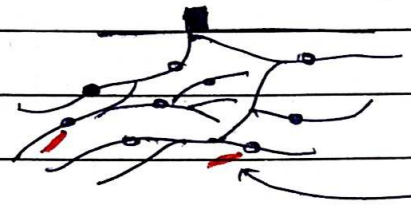
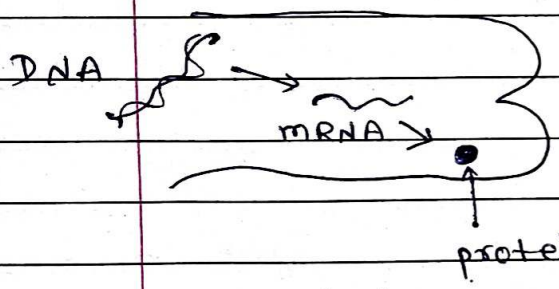
- Tobaco plants (pest - resistant)



Nematode
↳ Meloidegyne incognitia

infected tobaco plant
(root - knot disease)

cause

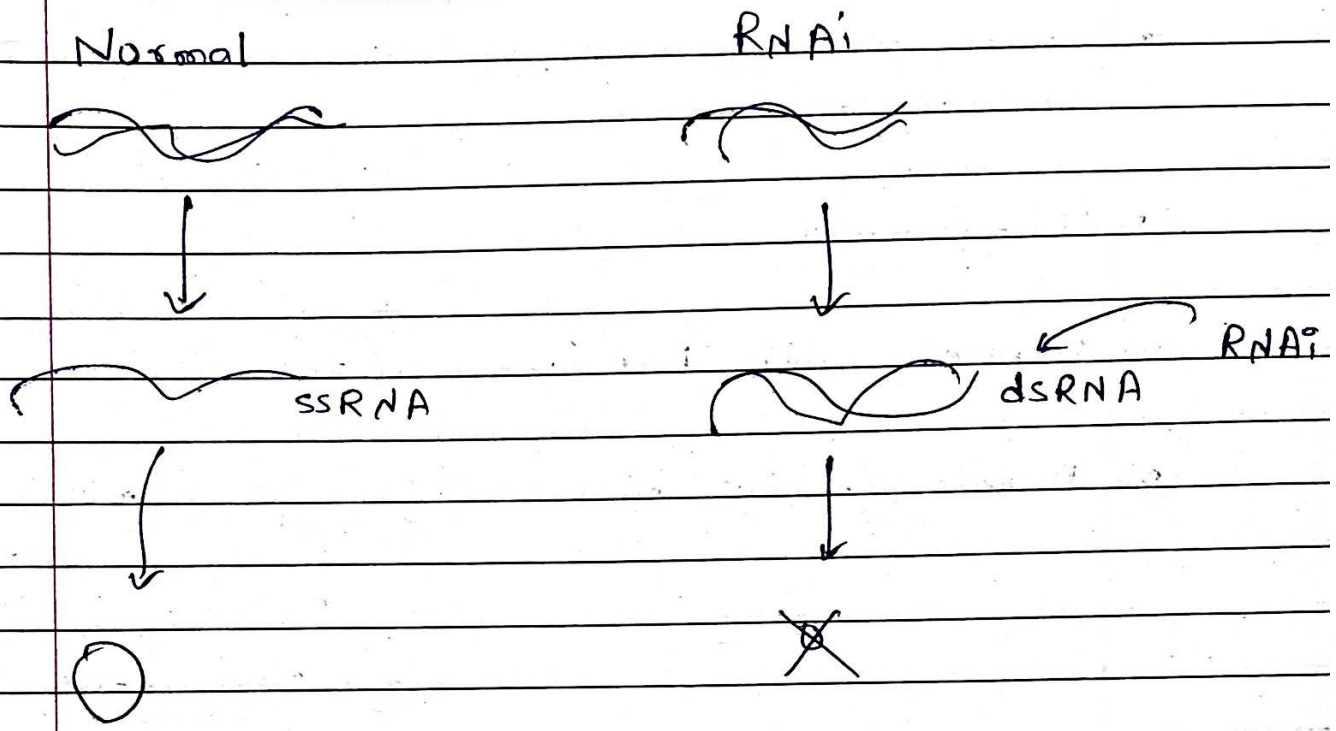


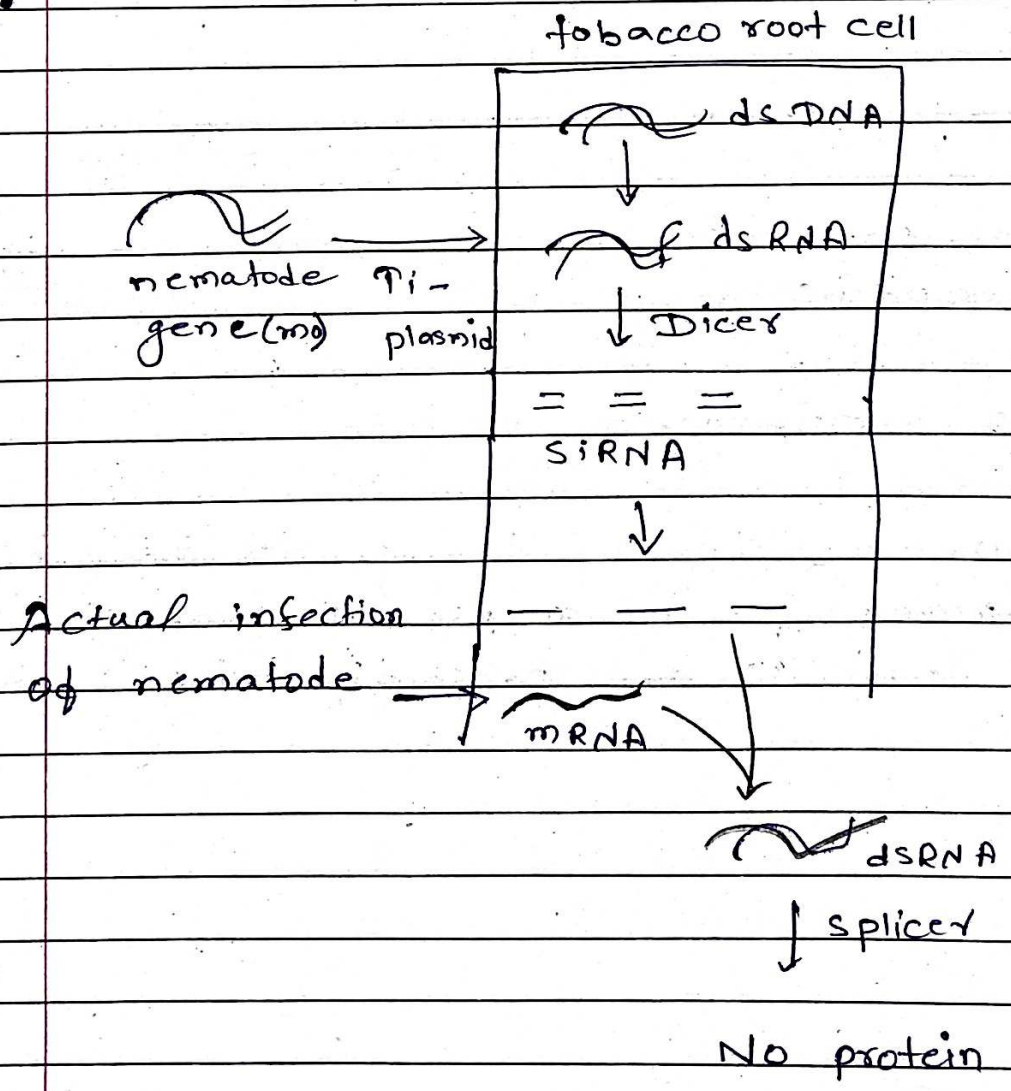
Nematode ↳ essential for feeding & survival

- Our motive stop translation of this specific protein. So that the nematode does not grow

↳ for this we will stop translation

↳ We will convert ssRNA into dsRNA, done by RNA interference / RNAi / mRNA silencing / anti - sense technology


Normal
RNAi
SSRNA
dsRNA
RNAi


tobacco root cell
dsDNA
dsRNA
nematode gene(mo)
Ti-plasmid
Dicer
SiRNA
Actual infection of nematode
mRNA
dsRNA
splicer
No protein

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Page _____

- There are 3 ways to introduce GOI in tobacco root cell

(1) Ti - plasmid

(2) Viruses with RNA genome (retro - virus)

(3) Mobile genetic elements/ transposon (replicate via RNA)

↓

"jumping gene"

* Application in Medicines

- Role of rDNA technology in medicine:

(1) Mass production of safe and more effective therapeutic drugs

(2) No immunological respone

Note:- 30 recombinant therapeutics have been approved for human use all over the world. In India 12 are presently being marketed

Date ___/___/___
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Diabetes

Diabetes mellitus
B-cell of pancreas
↓ secrete less
insulin

Diabetes insipidus
↳ vasopressin ↓
water reabsorb ↓
urination ↑

insulin ↓, sugar in blood ↑

- Insulin

→ In case of diabetes(D.M) patient take insulin from outside as the beta cells of pancreas donot produce enough insulin and the level of sugar is high.

→ Earlier insulin was isolated from pancreas of slaughtered cattle and pigs

↳ Disadvantage :- Cause allergy or other reaction

↳ Solution :- prepare insulin in lab with the help of rDNA technology

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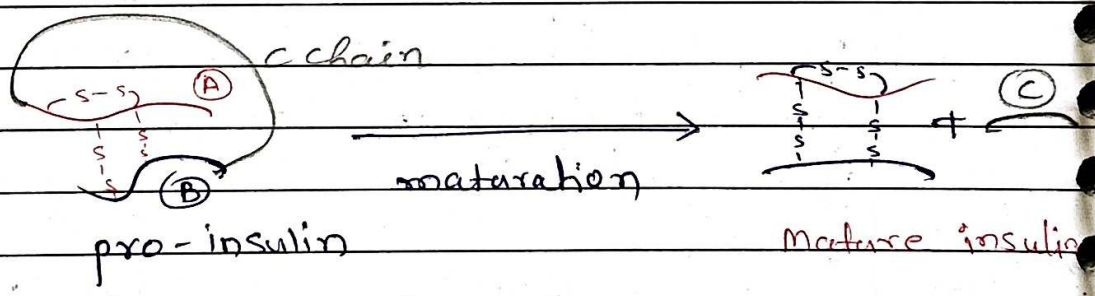
- Structure of insulin:

Insulin gene
↓
proinsulin (inactive)
↳ chain A(21aa) and chain B(30aa) are connected by chain C(31aa)

→ A and B chain are connected by 2 disulphide bond. Also one disulphide bond is present within A chain

→ During activation of pro-insulin, C chain is removed and mature (functional) insulin is formed



A & B = 2 disulphide bond
Within A = 1 disulphide bond

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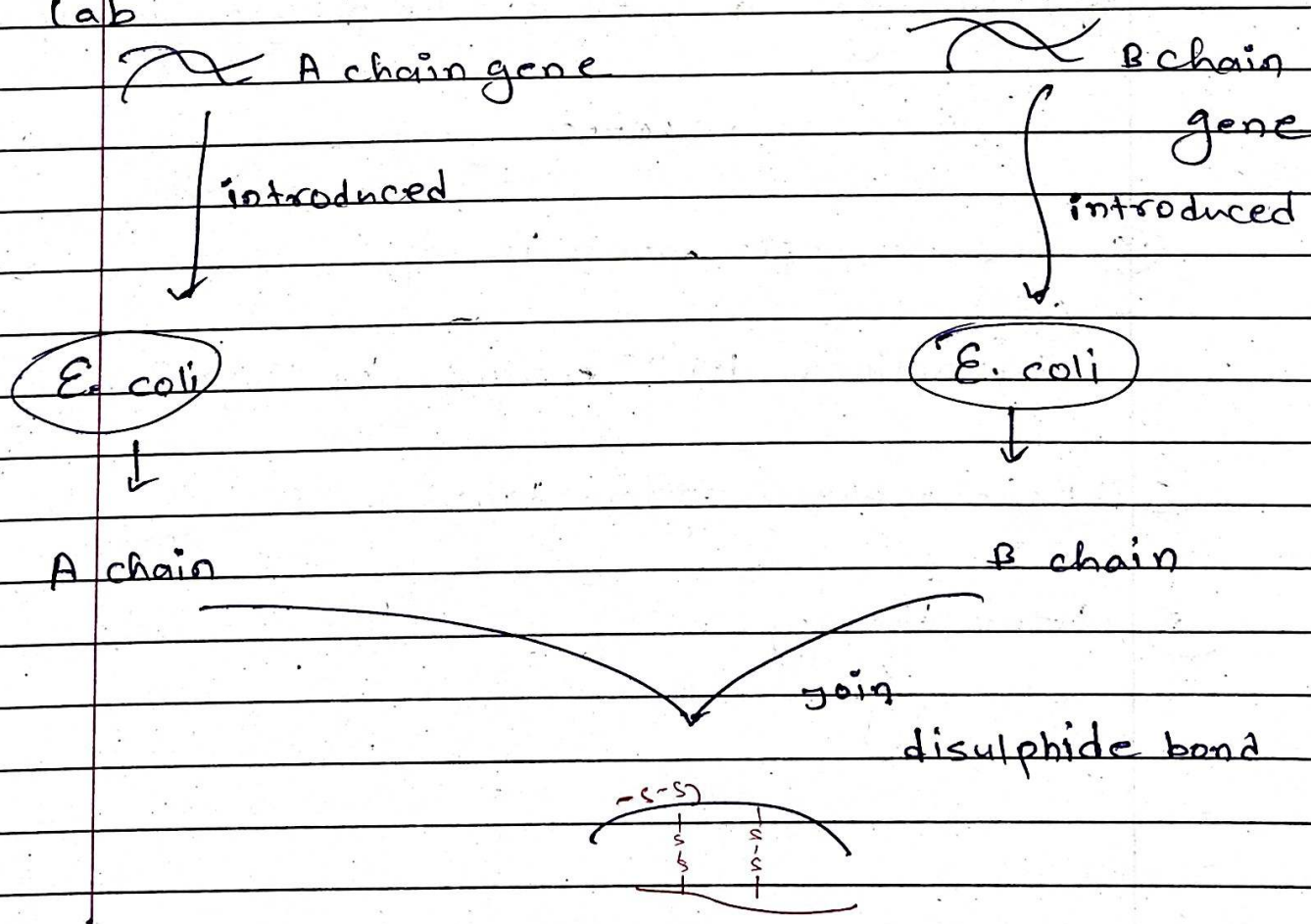
- But we can't produce genetically engineered insulin using E. coli because maturation or assembling of insulin is task

- In 1983 American company Eli lilly prepared synthetic gene for A chain and B chain. These gene were introduced in E. coli seprately. As a result A chain and B chain produced separately. At the end these 2 joins were joined by forming disulphide bonds

In this way Humulin was produced (1st GE insulin/hormone)

lab



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Gene therapy

→ It is collection of methods that help us to correct gene defect that has been diagnosed in child/embryo.

→ Here, normal gene is delivered to the individual to replace non-functional gene.

→ 1st time gene therapy was given to 4 year girl in 1990. This girl was suffering from SCID – ADA (severe combined immuno deficiency Adenosine deaminase enzyme).

→ ADA (by ADA gene) is necessary for immune functioning as well as lymphocyte development

Treatment of defect gene

1. Enzyme replacement therapy
   ↳ functional ADA enzyme by injection
2. Bone marrow transplant
3. Gene therapy

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- Gene therapy

Take blood from patient

↓

Separate lymphocyte

↓

Culture lymphocyte

↓

Introduce functional ADA (c-DNA) into lymphocyte, using retrovirus.

↓

GE lymphocytes returned back into patient's blood

- ADA gene isolate (ds)

↓

ADA RNA(ss)

↓

This ss RNA is ligated with disarmed retrovirus's genome (vector, RNA)

↓

This vector is introduced in host (lymphocyte) and deliver ss ADA RNA in lymphocyte

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ss RNA $\xrightarrow[\text{reverse transcription}]{}$ CDNA

CDNA integrated in lymphocyte DNA and codes for functional ADA enzyme.

Not complete cure; as lymphocytes have lifespan (not immortal)

periodic infusions of GE lymphocytes.

permanent cure for SCID-ADA:

If gene therapy given at early embryonic stage (totipotent stem cell)

9.01.26

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Molecular diagnosis

- Early diagnosis help us for effective treatment
- When symptoms appear, the conc of pathogen is high
- At low concentration of pathogen, no sympto appear.

- Conventional diagnosis
  - serum analysis, blood test, urine test etc
  - Early detection not possible

- for early ~~diagnosis~~ → detection ÷ rDNA tech, PCR, ELISA

Diagonsis

Early
- symptom ⊖
- PCR, ELISA
- pathogen concentration ↓

late
- symptom ⊕
- conventional diagnosic technique
- pathogen concentration high

- Window period
  - Time period b/w infection and symptoms appearness.

Date ___/___/___
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→ In PCR, pathogen specific primers are added. If multiplication occur meaning the pathogen is present

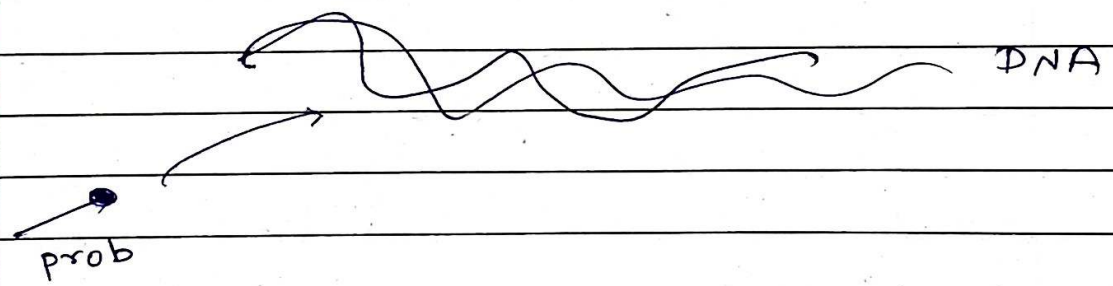
→ PCR is used in detecting HIV, to dectect mutation in gene, detect genetic disorder.

* Autoradiography

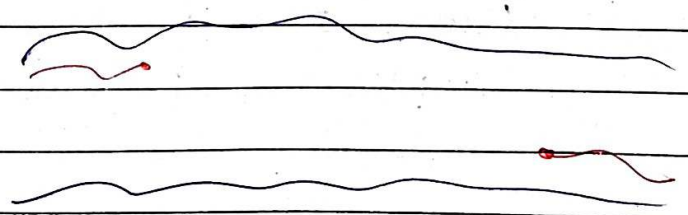
↳ To detect mutation in gene in a individual

CASE I

Normal ~~gene~~ DNA (no mutation)



- prob
  ↳ ssDNA/RNA complementary to normal gene tagged with radioactive material



↳ x-ray (light appear)

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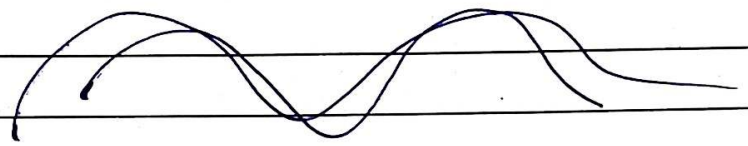
CASE II (mutated gene)

↳ Mutation



probe
↓
not bind
↓
not light
↓
Mutation

* ELISA

↳ enzyme linked immuno sorbent assay)

→

Reproductive Health

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* Introduction

- Reproductive health is not merely healthy reproductive organs and proper working of reproductive system.

- Reproductive health has broader aspects in other terms also like emotionally and socially.

- A/c to WHO, A person should be healthy in all aspects including reproductive health e.g. Physically, Emotionally, Behaviourally & socially

- India was among the first ~~cont~~ countries that initiate program aiming 'Reproductive Health' as social goal

- family program was initiated in 1951, later this program was renamed as RCH (Reproductive and child health ~~and~~ care)

- Aim of RCH program was to create awareness among people about reproductive health and reproduction

- Various other topics were also aimed like:- Adolescence, Reproductive organ, Reproduction, Menstruation, pregnency and care of mother, post natal care of child

- Hygiene during menstruation, sexually transmitted disease and gender equality.

- Through audio-visual, print media governmental and non-governmental agencies, awareness was spread among people

- Under RCH, following facilities were also provided :-
  (i) Infrastructural support
  (ii) Material support
  (iii) Medical expertise

- Sex education in school is promoted

- Role of teacher, parent, close relative and friends to create awareness about reproduction and related topics at individual level.

Amniocentesis

- Done b/w 16th – 20th week of pregnancy
- In this technique amniotic fluid is taken which contain fetal cells and dissolved substance
- These fetal cells are analysed and Karyotyping is done
  ↳ study of chromosomal pattern

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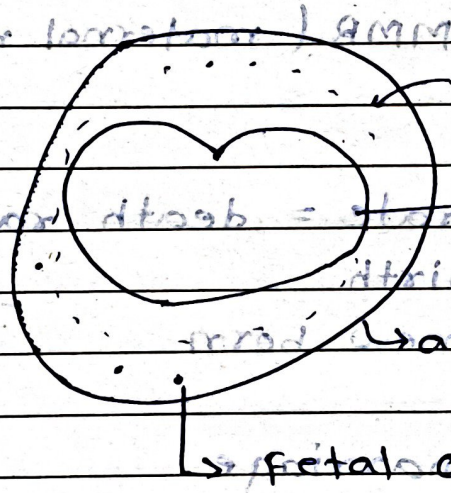
- Main aim of amniocentesis is to detect genetic disorders of fetal
  - down's syndrome (21st chromosome abnormal)
  - sickle cell anemia (11th chromosome abnormal)
  - Haemophilia/color blindness
  - Klinefelter's syndrome
- Amniocentesis was misused for sex determination which cause increase in female foeticide.
- Amniocentesis was illegally ban



* population explosion

- Rapid unlimited population growth
- Result in scarcity of food, water, employment also cause increase in crime, poverty etc
- population growth rate :- < 2% [20/1000/year] (a/c to 2011 census report)

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year	world population	India population
1900	2 billion	350 million
2000	6 billion	1 billion
2011	7.2 billion	1.2 billion

- Reason of population explosion :-
  (i) Increase members in reproducible age
  (ii) Decrease in death rate
  (iii) Decrease in IMR (infant mortality rate)
  (iv) Decrease in MMR (maternal mortality rate)

- Term :-
  - mortality rate = death rate
  - natal → birth
  - infant → new born

- legal age of marriage
  ↳ male = 21 years
  ↳ female = 18 years

- ~~So~~ SLOGAN
  ↳ Hum 2 Humare 2
  promoting small families

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* Contraceptive method

- Contraceptive methods are those methods which prevent pregnancy/conception.

- Characteristics of ideal contraceptive :-
  (a) user-friendly
  (b) Easily available
  (c) cheap
  (d) Reversible
  (e) effective
  (f) least or no side effect
  (g) should not interfere with sexual drive of user.

- There are many types of contraceptive available in market. Some categories are discussed below.

(a) Natural/Traditional method

→ In this method, chances of meeting of ovum and sperm is avoided

→ No chemicals, external devices are used in this hence, side effect is almost nil.

→ But chances of failure of contraception is high

→ It includes :-

(i) periodic abstinence/calender method
↳ Rhythm method

→ In this, the couple avoid coitus during 10th — 17th day of mentrual cycle
↳ fertile period

→ During this phase, chances of ovulation is high, which may result in fertilisation and pregnancy

(ii) Coitus interrupts / withdrawl method

→ During ejaculation, male withdraw his penis from vagina of female and avoid insemination.

no insemination
↓
no fertilisation
↓
no pregnancy

(iii) Lactational amenorrhea
↳ ~~Laction~~ ↳ absence of menstruation
↳ Lactation

→ During intense lactation, female do not ovulate, which further inhibit pregnancy

→ Maximum upto 6 months

→ Due to high level of prolactin, ovulation and menstruation is inhibited

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(b) **Barrier method**

→ In this method, physical meeting of sperm and ova is avoided by using a barrier

(i) **Condom**

→ Disposable
→ self - insertable (privacy to user)
→ Made of thin-rubber or latex sheath.
→ prevent transmission/spread of STD or AIDS during intercourse
→ Available for both

Male	female
→ cover penis of male	→ cover cervix and vagina of reproductive tract
NIRODH - popular brand	

(ii) **Diaphragm, Vault, cervical cap**

→ Cover cervix of female reproductive tract
→ use by female only

- Spermicidal jellies, foam, cream are used alongwith barrier method which increase contraception efficiency

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- Spermicidal chemical are those chemical which kill sperm
  eg. lactic acid, boric acid, zinc sulphate

(c) IUD (intra-utrine device)

→ It is inserted in the uterus of female by doctors, expert nurses through vagina.

→ It is widely accepted in India

→ Ideal contraceptive for female who wants delay pregnancy or space children

- Types of IUD:-

(i) Non-medicated IUD
→ Increase phagocytosis of sperm which uterus
eg. lippe's loop

(b) Copper releasing IUD
→ These IUD release Cu^{2+} (copper ions) that reduce motility and fertilising capacity of sper
→ e.g. CuT, Cu7 and multiload 375

(c) Hormonal IUD
→ Release ~~estrogen~~ and progestrone
→ make uterus unsuitable for implantation.
→ Make cervix hostile to sperm
→ eg. LNG 20, progestasert

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(d) Oral contraceptive pill
↳ well accepted by female
→ Taken in the form of tablet orally so, now as pills

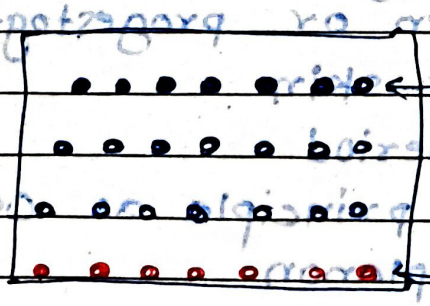
→ Oral contraceptive pill have

either progestogen alone

Combination of progestogen & estrogen
eg:- Mala D, Mala N

- These pills cause :-
  - inhibition of ovulation
  - inhibit implantation
  - alter quality of cervical mucus causing retard ~~entery~~ entry of sperm

Q How to take pills?
- Started within 5 days of menstrual phase
- Take regularly for 21 days
- Then gap of 7 days is there in which again Menstruation occur
- The cycle is continued till conception is prevented



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- Saheli (Developed in CDRI - lucknow)
→ non-steriodal pill / Non-hormonal pill
→ Once a week pill
→ Composition - Centchroman
→ block estrogen receptor on uterus
↓
estrogen can't bind to its receptor
↓
No proliferation of endometrium
↓
No implantation
→ No side effect

(e) Injectable and Implants

- Injectable
→ injections having progestogen or progestogen - estrogen combination
→ Work on same principle as OCP
→ eg. Depo-provera

- Implants
→ Silicon stick having hormonal combination either progestogen or progestogen - estrogen
→ implanted under skin
→ long effective period
→ Work on same principle as OCP
→ eg. Norplant, Implanon.

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* Emergency Contraceptive

- pills having progestogen or estrogen – progestogen combination, IUDs can be used as emergency contraceptive within 72 hours of coitus

- Reason of using emergency contraceptive :-
  (i) failure of contraceptive used during coitus
  (ii) In case of rape
  (iii) If couple is not mentally ready for pregency

- E.g of emergency pill :- I pill, Unwanted 72

* Surgical method/termination method/sterilization

→ permanant method
→ highly effective
→ less reversibility
→ Done through surgery
→ Tranfer of gamete is blocked

Surgery

male → vasectomy

female → Tubectomy

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- Vasectomy
→ Cut in vas-deferens & tied seperately
→ Incision in scrotum
→ Semen contain no sperm
→ spermatogenesis continues

- Tubectomy
→ Cut in fallopian tube and tied sepretely
→ inclusion in abdomen or through vagina
→ Oogenesis continues
→ Mentrual cycle continues

* Side effects of contraceptive :-
(a) Irregular mentrual cycle
(b) Nausea/vomitting
(c) Breakthrough bleeding
(d) Breast cancer, reproductive tract cancer
(e) Abdominal pain.

* Medical Termination of pregnancy (MTP) or Induced abortion

- MTP is a procedure in which pregnancy is terminated voluntary before full term.

- It should be legal or illegal is a matter of debate because of social, ethical, religious belief.

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→ It is safe during 1st trimester and riskier in 2nd trimester.

→ In India, MTP was legalised in 1971, under certain condition to avoid its misuse and to decrease case of female foeticide.

Q. Why MTP?
→ When foetus is abnormal
→ When life of mother or foetus is in danger
→ In case of rape victims
→ When female is not ready mentally or physically for pregnancy

• In a year, all over world 45 – 50 million MTP done
↓
$\frac{1}{5}$th of this concived/pregnancy occur

* STD (sexually transmitted disease)

• STD also called sexually transmitted infection (STI), reproductive tract infection (RTI) and ~~va~~ Veneral disease (VD)

• STD are those disease which is transmitted from one ~~pere~~ person to another through sexual contact.

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STD

Curable	Uncurable
gonorrhea	AIDS
Syphilis	genital herpes
genital warts etc	Hepatitis-B

- Hepatitis B and AIDs can also be transmitted through
  (i) sharing of injection needles, surgical instrument
  (ii) Blood transfusion
  (iii) from infected mother to foetus.

- Early detection and early treatment play vital role in treating STDs

- Early symptoms (minor) :- itching, fluid discharge, swelling, slight pain in genital region.

- Late symptoms (complicated) :- PID (~~pelv~~ pelvic inflammatory disease), abortion, still birth, ectopic pregnancy, infertility, reproductive tract cancer.

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- Ectopic pregnancy ÷ pregnancy in which implantion is done at other place than uterus.

- 15-24 years → age in which chance of STD is high

Q. How to prevent STD ?
(i) Avoid sex with unknown/multiple partners.
(ii) Always use condom in uprotected coitus
(iii) In case of dout, consult a doctor and get a complete treatment.

- Bacterial STDs — pathogen
(i) Gonorrhoea — Neisseria gonorrhoeae
(ii) Syphilis — Treponena pallidum
(iii) Chlamydiasis — Chlamydia trachomatis

- Viral STDs — pathogen
(i) Genital Herps. — HSV (herpes simplex virus)
(ii) Hepatitis-B — Hepatitis-B virus
(iii) Genital Warts — HPV (human papillomavirus)
(iv) AIDS — HIV ~~HPV~~ (human immune - deficiency virus)

- Protozoal STDs — pathogen
Trichomeniasis — Trichomonas vaginalis

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* Infertility

- When a couple is not able to produce children even after unprotected sexual cohabitition of 1 or 2 years

Infertility

primary infertility
→ no reported pregnancy in past

secondary infertility
→ pregnancy occured in past, problem in concieving further

- Reason of infertility ÷ Congenital, physical, drugs, immunological, psychological etc.

- In case of infertility, couple visits doctor to and get treatment. There is a possibility that even after treatment, couple is not able to produce children. Then they go for ART (assisted reproductive technology)

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- In-vitro fertilisation

→ fertilisation outside body (in lab).

(a) Test tube ~~bad~~ baby program

donor/husband → collect → sperm

donor/wife → collect → ova

sperm + ova → induce to fertilize in a test tube or petridish

→ zygote formed

→ Embryo tranfer

upto 8 blastomers
- Embryo is tranfered in fallopian tube

ZIFT
Zygote intra fallopian tranfer

more than 8 blastomers
- Embryo is tranfered in uterus

IUT
intra-uterine tranfer

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(b) ICSI
→ intra cytoplasmic sperm injection
→ In this sperm is directly injected into ovum
→ In-vitro fertilisation.

• In-vivo fertilisation
→ fertilisation inside female body

(a) GIFT (gamete intra fallopian tranfer)
→ If mother is not able to produce ova, then ova from donar is trandered in the fallopian tube of mother
→ In-~~vit~~ vivo fertilisation

(b) AI or IUI (intra uterine insemination)
↳ artificial insemination
→ If male partner is unable to inseminate his semen or have low sperm count, then the semen from husband/doner is artificially inseminated in the vagina or uterus of female.

• Disadvantages of 'ART' :-
→ very expensive
→ available in few centres only
→ require precise handling and expertise

Note:- Legal adoption is the best way for the couple who want to become parent (but due to infertility, they are not able)

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- Hysterectomy ÷ Surgical removal of uterus.